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EDITORIAL

1956, OUR Golden Jubilee year, has been an eventful one for this Journal, and one on which we may look back with pride. The pioneer efforts of the Journal, its continued spirit of independence and its success in promoting knowledge of tuberculosis and diseases of the chest in the preventive, social, diagnostic and therapeutic spheres has received extensive recognition by our contemporaries in this country, the Dominions, the United States and many European countries. It goes without saying that we are duly appreciative of these many tributes.

Our constant endeavour to cover the whole of thoracic medicine has won widespread approval: the Chief Medical Officer of the Ministry of Health, Sir John Charles, in his foreword to our Golden Jubilee issue, commented, " Unlike every other specialist organ, it has enlarged its sphere and widened its influence and interest. Instead of catering for those who would know ' more and more about less and less,' it now prints more and more about more and more—a trend as refreshing as it is unusual in these days."

Sir Robert Young, C.B.E., our doyen of chest medicine, now in his eighty-sixth year, himself a valued contributor and a guest of honour at the Golden Jubilee Dinner, paid tribute to " the outstanding achievement of the Journal, and the courage, vision and enthusiasm on the part of the first Editor, Dr. Kelynack, and the publishers, in starting a Journal in a special field in 1906, when specialisation was at a very early stage of evolution."

We have constantly reiterated that we aim at a comprehensive chest service, embracing the whole of thoracic medicine, including respiratory tuberculosis, integrated with other branches of general medicine—prevention, diagnosis, treatment, after-care and rehabilitation being co-ordinated as one continuous process.

It is generally recognised that advances in all branches of medicine in the present century, and especially in the last decade, make some degree of specialisation inevitable. In no sphere of activity have these advances been greater than in thoracic medicine. Nevertheless, narrow specialisation within a limited field is fraught with danger both to our own profession and to the community. It remains more than ever necessary for the patient to be studied as an entity, so that the part shall not be wrongly interpreted as the whole. Walshe's contention that " the specialist must cling to the foundations of medicine and orient them " must be constantly borne in mind.

Crighton Bramwell, in his admirable Harveian Oration for 1956, referring to the risks of specialisation, quoted from Osler's presidential address to the Classical Association in 1919: " The extraordinary development of modern science may be her undoing. Specialism, now a necessity, has fragmented the specialities themselves in a way that makes the outlook hazardous. The workers lose all sense of proportion in a maze of minutiae. Everywhere men

are in small coteries, intensely absorbed in subjects of deep interest but of very limited scope . . . applying themselves early to research, young men get into backwaters far from the main steam. They quickly lose the sense of proportion, become hypercritical, and the smaller the field the greater the tendency to megalocephaly." Similarly, Himsworth, in his Linacre Lecture for 1955, " the experts in a particular field must be sufficiently skilled in the other disciplines concerned to be able to talk the language and appreciate the outlook of those other experts whose help is required." Our aim, therefore, in future activities will be to guard against the risks of a too narrow specialisation, and to ensure that we integrate our speciality with general medicine, for disease in the lungs alone can be an index of systemic disease.

Certain changes in the Editorial Board have to be recorded: we deeply regret the retirement of our stalwart guide and counsellor, Professor Charles Cameron, C.B.E. An appreciation of his work in the Chair of Tuberculosis at Edinburgh was published in our columns in 1952 (April issue) by his colleague, Professor Melville Dunlop. We take some satisfaction, however, from his assurance that we may still on occasion avail ourselves of his help. His place is being taken by Dr. R. Y. Keers of Tor-na-Dee and Glen o' Dee Sanatoria, who will represent Scotland on the Editorial Board. His position, as an expert clinician in tuberculosis and diseases of the chest, is a fine one, and we welcome him warmly. We are also happy to welcome Professor A. Leslie Banks, Professor of Human Ecology in the University of Cambridge. His reputation as an expert in the sphere of social and preventive medicine will add lustre to the Journal.

Finally, may we humbly appeal to our numerous contributors: (*a*) To read the Notice to Contributors on the inside back cover of the Journal. Guidance on the mode of presentation of their manuscripts will ensure conformity with the style of this Journal. It will also avoid unnecessary labour on their part and on the part of the Editor and the Editorial Board. (*b*) To prune ruthlessly, owing to great pressure on our space. It is imperative for contributors to calculate how many words can be deleted without omitting any essential information. Might we, with great respect, draw attention to an observation by one of our early contributors, the late Sir Clifford Allbutt: " The man of science ought best to know that style and matter can no more be dissociated than skin and bone; but if we write clumsily, loosely or disjointedly, our thoughts are accordingly."

Editors and Editorial Boards are rightly jealous of the reputation of their Journals, and have a considerable responsibility towards their readers. If contributors will recognise these fundamental principles, they will help enormously towards the smooth running of the Journal.

May the recent celebration of our Golden Jubilee help towards the attainment of our future goal, through the goodwill and co-operation of all concerned.

CHANGES IN THE FUNCTIONAL RESIDUAL CAPACITY WITH DEEP BREATHING

IN NORMAL AND EMPHYSEMATOUS SUBJECTS

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Measurement of the functional residual capacity is less easy to perform than spirometry, so that it is not undertaken as often as the estimation of the vital capacity in the assessment of lung function. It is however of importance, since the functional residual capacity represents the volume by which the tidal air is diluted, and so changes in its volume may be expected to affect the rate of gas mixing in the lungs.

Bernstein (1954) has shown that inflation of the rabbit's lung *in vivo* can lead to an opening up of previously closed alveoli. Anæsthetists are familiar with this phenomenon in man. It was therefore of interest to discover whether the functional residual capacity was increased after a subject took a few vital capacity breaths.

Method

The technique used followed that of Bates and Christie (1950) with certain modifications which have been described by Buxton and D'Silva (1956). All subjects were examined in the sitting position.

The normal group consisted of 20 healthy medical students aged 18-27 years, and in addition 20 patients with pulmonary emphysema were studied whose ages ranged from 35-63 years (mean 48·8, S.D. 7·4).

Experimental Results

Normal Subjects

The mean functional residual capacity of the normal group of 20 subjects was 3·76 litres (range 2·2-5·7, S.D. 0·78). The time taken for " 63·2 per cent. mixing "—*i.e.*, the time constant of the mixing curve (Buxton and D'Silva, 1956)—was significantly (r=0·54) though not closely related to the size of the functional residual capacity (Fig. 1).

It has been demonstrated that the minute ventilation and the time constant are closely related (Buxton and D'Silva, 1956) in a hyperbolic form for the group of normal subjects breathing with minute ventilations ranging from 6-45 litres. If the results are plotted not as total minute ventilation but as minute ventilation per litre of functional residual capacity, the same type of relationship holds (Fig. 2) with a correlation coefficient of 0·96.

One subject performed the mixing test under the standard conditions. At the end of the experiment the helium percentage was read and the subject, still connected to the circuit, was asked to take several vital capacity breaths.

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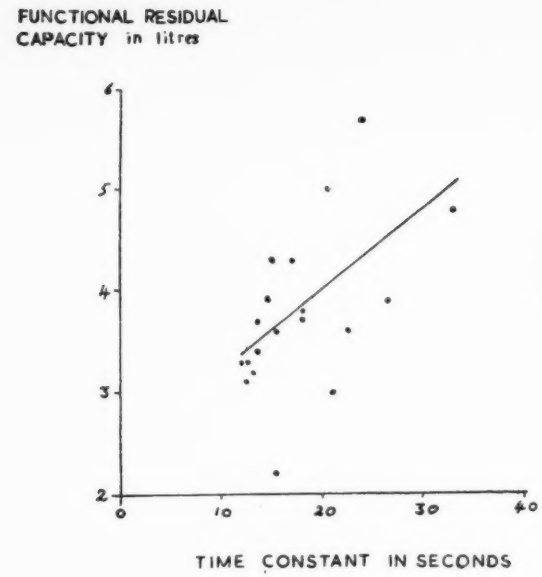

FIG. 1.—The relationship between the functional residual capacity and the time constant of the mixing curve in normal subjects.

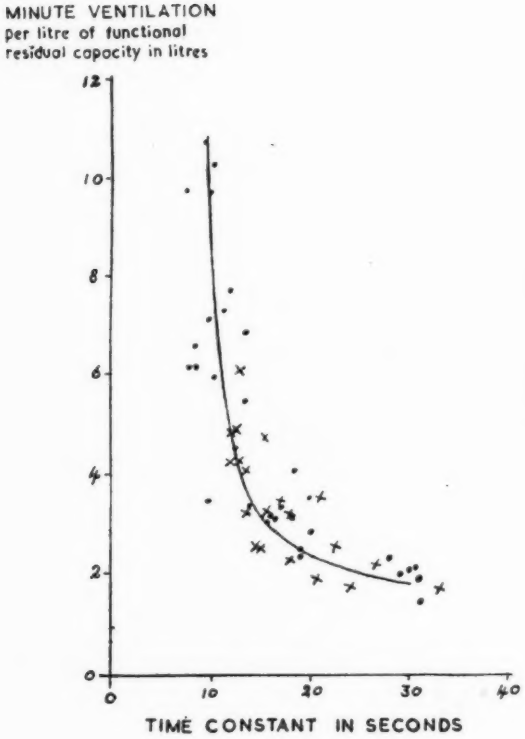

FIG. 2.—The relationship between the minute ventilation per litre of functional residual capacity and the time constant of the mixing curve. The crosses represent the results when the subject was breathing normally and the full circles were obtained when the breathing was controlled.

After these deep breaths he resumed normal breathing, and a few minutes later the helium percentage was again read. From these two readings two values for the functional residual capacity were calculated. The test was repeated on successive days on the same subject so that ten pairs of observations were available. It was found that the mean functional residual capacity as usually performed was 3·84 litres (S.D. 0·26); this was increased to 4·74 litres (S.D. 0·38) by the deep breathing. The difference between the two figures is highly significant ($P<0.01$). The mean values for the ratio of the residual capacity to the total lung capacity under the same conditions were 33·4 per cent. (S.D. 3·1) and 46·4 per cent. (S.D. 4·8) respectively, a difference which was very highly significant ($P<0.001$).

When each of 16 medical students, taken in chronological order from the 20

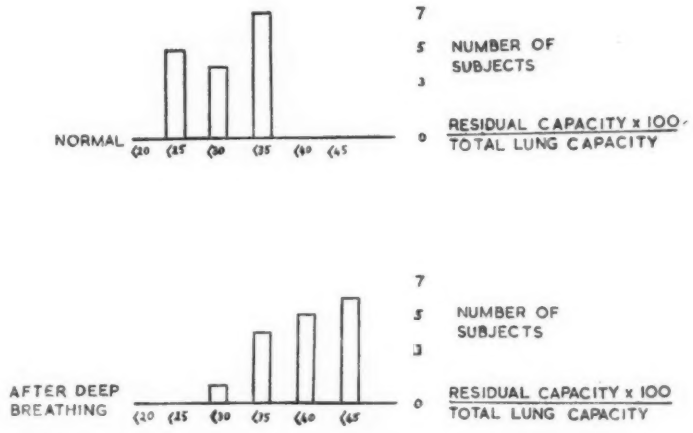

FIG. 3.—The figure shows the distribution of the percentage ratio of the residual capacity to the total lung capacity in the normal group. The upper histogram was obtained from tests when breathing was normal, the lower one after deep breathing.

in the group, performed the test once, the mean value for the functional residual capacity rose from 3·65 litres (S.D. 0·57) to 4·28 litres (S.D. 0·58), a difference which was highly significant ($P<0.01$). The ratio of residual capacity to total lung capacity increased from 28·6 per cent. (S.D. 4·7) to 37·2 per cent. (S.D. 5·2), which was a very highly significant difference ($P<0.001$). This change is illustrated in Fig. 3.

Patients with Emphysema

The 20 patients with emphysema had a mean functional residual capacity of 4·75 litres (S.D. 1·76), which was probably significantly greater ($0.05>P>0.02$) than that of the normal controls. The time constants of the mixing curves of the patients were related to the size of the functional residual capacity ($r=0.5$) as closely as in the young normal group, though the time constants

were longer and the values for the functional residual capacity were somewhat greater. But these patients differed from the young control group in one important respect: when the minute ventilation per litre of functional residual capacity was plotted against the time constant, the observations did not fall on the curve for normal subjects (Fig. 4). It is reasonable to deduce from this that the inefficiency of mixing cannot adequately be explained on the basis of an increased functional residual capacity alone.

In severe cases of emphysema, deep breathing involves considerable effort. This makes it difficult to obtain results comparable to the normal group for the effect of vital capacity breaths on the functional residual capacity. From those experiments which were technically satisfactory, there was a small increase in the functional residual capacity of 0·18 litre: this was not statistically significant.

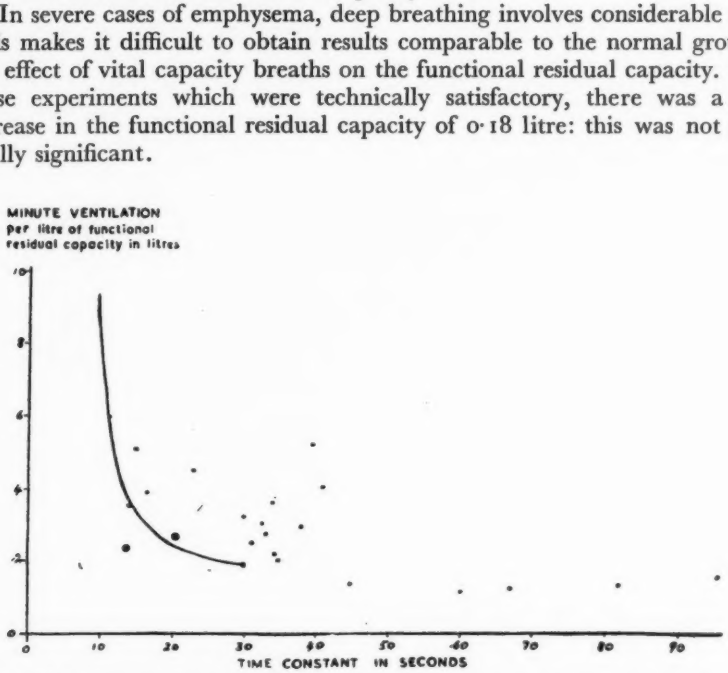

FIG. 4.—The observations for the minute ventilation per litre of the functional residual capacity and the time constant of the mixing curve in the patients with emphysema. The curve obtained from the normal subjects and shown in Fig. 2 is superimposed.

Discussion

There is no evidence to suggest that in normal subjects deep breathing alters the expiratory reserve volume, and since deep breathing increases the functional residual capacity, it follows that the residual capacity must be affected. The significance of this lies in the fact that the residual capacity expressed as a percentage of the total lung capacity is often used as an aid in the diagnosis of chest disease, particularly of emphysema. From this series of experiments on young subjects, the upper limit of normality of this fraction is 38·2 per cent., a figure which is similar to those quoted by Hurtado and Boller (1933), Bates and Christie (1950), and Needham, Rogan and McDonald (1954), amongst others. If, however, the fraction residual capacity divided by total lung capacity was determined soon after the subject had breathed deeply,

over 40 per cent. of the present young controls would have appeared to be abnormal.

An increase in the volume of the functional residual capacity may be expected to retard the process of gas mixing. Reference to Fig. 2 shows that when the minute ventilation per litre of functional residual capacity is 4 litres, any increase in ventilation will be of little significance in improving the efficiency of gas mixing, but any decrease will lead to an impairment of efficiency.

It is a reasonable supposition that the purpose of this increase in the functional residual capacity may be to provide a greater respiratory surface for gas exchange in response to a ventilatory demand. The fact that the functional residual capacity does not increase with deep breathing in patients with emphysema may be regarded as an expression of the absence of any pulmonary reserve in these cases. Although the volume of the functional residual capacity at rest may be increased, and the observations presented suggest that the range is wide, our results are in agreement with the view that the volume change is not the major cause of the impairment of gas mixing in emphysema.

Summary

A group of 20 young normal subjects and 20 patients with emphysema was studied.

On deep breathing the functional residual capacity was significantly increased in the young control group but not in the patients with emphysema. The significance of this finding is discussed.

These investigations were undertaken during the tenure of a London Hospital postgraduate Fellowship.

It gives me great pleasure to acknowledge the help of Professor J. L. D'Silva. The author is indebted to Mr. G. Walter and the many subjects who have assisted him.

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DIAGNOSIS AND INCIDENCE OF SARCOIDOSIS*

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Owing to our lack of knowledge regarding the causation of sarcoidosis and the resulting impossibility of giving a precise definition of the morbid process, it is difficult to deal with the question of diagnosis. While at present, on histopathological and clinical grounds, we regard sarcoidosis as a morbid entity, we must bear in mind that our definitions are imperfect and may need revision as new evidence concerning the ætiology arises.

Pathology

" Pathologically sarcoidosis is characterised by the presence in any organ or tissue of epithelioid cell tubercles, with inconspicuous or no necrosis, and by the frequent presence of refractile or apparently calcified bodies in the giant cells of the tubercles. The characteristic lesions may be replaced by fibrosis, hyalinisation, or both " (Ricker and Clark, 1949).

It should be pointed out that this histopathological picture is not pathognomonic of sarcoidosis. Similar tissue changes may be found in several morbid conditions of different ætiology—*e.g.*, in bacterial infections like tuberculosis, leprosy and tertiary syphilis; in fungus infections such as coccidioidomycosis, histoplasmosis and moniliasis; and also in lesions due to the presence of foreign bodies, foremost among which are berylliosis and silicosis.

The Clinical Picture

Appraisal of the variable clinical picture is difficult owing to the fact that the sarcoid granulations may be present in practically any one of the organs and show considerable individual variation. Nevertheless certain features can be distinguished which are more or less regularly encountered in the groups of cases considered here.

This paper is confined to pointing out some characteristics which are useful aids in making the diagnosis. In doing so I shall first discuss the difference between the initial and the chronic stages (Löfgren and Lundbäch, 1952; Löfgren, 1953; 1955).

Primary Sarcoidosis

The primary sites of involvement open to clinical observation are the lungs and the associated mediastinal lymph nodes. Especially characteristic of the clinical primary stage is the occurrence of large, bilateral, comparatively symmetrical, polycyclic hilar lymphomas, associated in one-third of the cases

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with paratracheal lymphomas, usually on the right side. Not infrequently the onset of illness is heralded by erythema nodosum. Owing to the falling incidence of primary tuberculous infection early pulmonary sarcoidosis seems nowadays to be the most common cause of erythema nodosum in Scandinavia. Further, frequent signs of arthritis occur in the early stage of sarcoidosis, particularly in the shape of swelling of the ankles, due apparently to periarticular œdema. For this reason such cases are not infrequently diagnosed as rheumatic polyarthritis until X-rays of the chest are taken.

The prognosis of early pulmonary sarcoidosis is generally favourable; in more than 90 per cent. of the cases associated with erythema nodosum the hilar lymphomas and supervening parenchymal lesions will subside within one to two years.

In about half the cases with large bilateral hilar lymphomas supraclavicular lymph nodes can be noted on palpation, particularly on the right side, and these are accessible for biopsy. Even in instances where lymph nodes cannot be felt on palpation scalene node biopsy will sometimes yield histopathological evidence. The sarcoidosis nodes are fairly soft and freely mobile, without signs of periadenitis. The cut surface is yellowish and greasy, without appreciable necrosis. As a rule naked-eye inspection at this stage will provide a provisional diagnosis and exclude both tuberculosis and Hodgkin's disease.

If there are pronounced signs, and in particular if the hilar lymphomas are large, the clinical picture of primary sarcoidosis scarcely gives rise to confusion with other morbid conditions. The disease which, radiologically, most closely resembles early sarcoidosis would seem to be coccidioidomycosis, which, however, has a geographically limited incidence and can also be diagnosed by demonstration of the causative fungus. In cases where the lymphomas are smaller, tuberculosis claims first consideration in differential diagnosis. The tuberculin test and examination for the presence of the tubercle bacillus are naturally required for elucidation in this respect. It should, however, be emphasised that the usefulness of the tuberculin test is restricted, in that patients with early sarcoidosis will respond to tuberculin in 50 per cent. of cases, although not as a rule until amounts as large as 0·1 mg. or 1·0 mg. are used in the Mantoux test. In both generalised and chronic cases the tuberculin anergy may be more pronounced, yet even in such instances it is relative and not absolute. Various authors quote rates of tuberculin-positivity of from 3 per cent. to 35 per cent. in such case series.

Even where the generalised forms of sarcoidosis are concerned, pulmonary involvement is predominant (Ricker and Clark, 1949; Longcope and Freiman, 1952).

Chronic Pulmonary Sarcoidosis

The most conspicuous and often the only subjective symptom of chronic pulmonary sarcoidosis is dyspnœa. Usually there is no fever, and the erythrocyte sedimentation rate is frequently normal. The radiograph may possibly show persisting hilar lymphomas, usually less conspicuous than in the acute stage. But, first and foremost, parenchymal changes are apparent which present either as shotty or slightly more patchy, scattered densities or as reticulation and linear markings. Characteristic of the persisting parenchymal changes,

particularly in the larger densities, is the fibrosing tendency, which may result in pronounced emphysema. Differentiation from tuberculosis, fungus infections and pneumoconioses may often be very difficult.

The development of extrapulmonary manifestations of sarcoidosis may settle the diagnosis. Characteristic signs of this type are *e.g.* uveoparotitis and lesions involving the skin, mucous membranes and osseous system. The cutaneous lesions may sometimes be quite inconspicuous, presenting as reddish-brown nodules of split-pea size or even smaller, which may easily escape the patient's observation. A site of predilection is in old scars, which should, therefore, be carefully scrutinised (Löfgren *et al.*, 1954). If the patient complains of nasal obstruction the cavities of the nose and the nasopharynx should be examined; in such cases one may find polypus-like brownish-yellow infiltrations with the typical histopathological picture.

Recently, increasing attention has been paid to involvement of the kidneys by sarcoidosis. If the disease is treated with vitamin D_2, hypercalcæmia in conjunction with renal damage will not infrequently ensue. Hypercalcæmia, with or without evidence of renal damage, however, has been noted in several instances without previous calciferol treatment. The renal involvement, whose histopathological basis is a specific interstitial nephritis, may not give rise to appreciable symptoms in mild cases. In more severe cases it is manifested by impaired renal function. It is a remarkable fact that in instances of generalised sarcoidosis the blood uric acid level has often been found to be elevated even in cases where the non-protein nitrogen was normal or but slightly increased (Löfgren, 1955). This phenomenon, for which there is so far no explanation, may be of interest from the standpoint of differential diagnosis and is the object of further study.

Of other changes in blood chemistry there may be mentioned hyperglobulinæmia, which is common in the generalised form of the disease but is usually absent in mild or inactive cases.

A characteristic feature of chronic sarcoidosis, which may to some extent be helpful in diagnosis, is the absence of subjective symptoms despite fairly extensive changes. For the rest, two tasks are essential in making the diagnosis: on the one hand, to rule out other diseases with similar clinical pictures, especially tuberculosis; on the other, to obtain support for the clinical suspicion of sarcoidosis by means of histopathological study.

The material chiefly used for biopsy is derived from lymph nodes, which, in the early stage, as has already been pointed out, will be most certainly found in the supraclavicular fossa but, in the chronic stage, can be successfully sought in other regions. Most accessible to biopsy are sarcoids in the skin and mucous membranes. Specimens taken from the tonsils may at times yield positive findings, though later workers have been less successful with this material than Schaumann was in his cases. Typical pictures may be found in the bronchial mucosa as well as in internal organs such as the liver and kidney.

In those instances where patients with suspected sarcoidosis have to undergo operations, histopathological study of organs or portions of organs, which possibly are removed, should never be omitted. For example, in such cases we have found specific changes in the lung, thyroid, gall-bladder and stomach after excision of those structures.

Incidence of Sarcoidosis

As regards the incidence of sarcoidosis, it is impossible at present to form a clear impression. As will have emerged from the foregoing, there are two definite reasons for this uncertainty.

First, the diagnosis is not based upon ætiological factors but to a certain extent is influenced by subjective appraisal.

Second, in may instances symptoms are so scanty and mild that the disease is disclosed only on some routine examination.

The disease is sometimes stated to be on the increase. This may possibly be true, but the apparent increase may be only an impression due to more frequent diagnosis of the condition, partly through the ever-increasing use of routine radiography of the lungs and partly through improved differential diagnosis, in particular from tuberculosis.

Cases of sarcoidosis have been reported from most of the European countries, from the United States, Canada, Brazil, Argentina, North and South Africa, Japan and Australia. It is generally stated that the incidence is greatest in the Scandinavian countries. Whether, in that case, it is due to racial predisposition or local factors, climatic or physiographic, is obscure.

The most reliable estimate of the incidence of sarcoidosis is obtained from routine examination of large population groups. Computed on this basis for some regions of Sweden, it is as follows: Alvsborg County, 5/10,000; Jämtland County, 14/10,000. The Stockholm series disclosed for men the incidence rate 3/10,000, and for women 5/10,000. In the age group 25-29 years, where the incidence is highest, the rates were 9/10,000 and 11/10,000, respectively.

In so far as the incidence rates quoted relate to cases of chronic pulmonary sarcoidosis, they provide some information as to the occurrence of sarcoidosis. Since mass X-ray examination does not completely reveal the frequency of past tuberculous primary infection, the evidence as to the incidence of primary pulmonary sarcoidosis is incomplete. It is known that the major proportion of the hilar lymphomas, which are discovered by miniature radiography and are typical of sarcoidosis, recede fairly rapidly, and it is therefore to be expected that many of the cases assessed as normal, either a longer or shorter time before the examination in question, had passed through a similar phase of illness or will do so later on. This implies that the benign primary stage of sarcoidosis is far more common than the results of a single mass X-ray survey reveal.

Geographical and Racial Variations

Of special interest are incidence ratios which might provide information as to the pathogenesis of sarcoidosis. For example, according to many workers the disease is more common among rural than town populations.

In the United States interesting studies were made of the sarcoidosis material collected during the second World War by routine examination of military personnel. This was a series including 350 patients. In a first report by Michael *et al.* (1950) there appeared as the most striking features, on the one hand, the previously known high incidence among the negro population and, on the other, the geographical and rural distribution of birthplaces of the patients.

When the material was further analysed (Gentry *et al.*, 1955), the previously ascertained predominance of negroes was confirmed, and the ratio of negro to white cases was stated to be 18 to 1. The concentration of sarcoidosis cases in the South-eastern States applied to both whites and negroes and could not be attributed only to the accumulation of negro population within those regions.

It was found that the incidence density of sarcoidosis was closely related to the physiographic area known as the Atlantic and Gulf Coastal Plain. Until relatively recent geological times this area was covered by the sea. Its western-most limits are defined by the former coastline, now known as the " Fall Line."

The authors discuss whether the observed geographic localisation of the disease is the result either of the presence of a highly favourable environment for the growth, propagation or transmission of an ætiological agent or agents, in areas within the South-eastern States, or of an alteration in the susceptibility of the population in these areas which predisposes them to the action of some agent that elsewhere might possess a very low-grade or altered pathogenicity. Of interest in this connection is the fact that certain fungus diseases, such as coccidioidomycosis and histoplasmosis, have a similar geographical localisation.

Age

The incidence of sarcoidosis also shows age variations. According to the literature the disease is exceedingly rare in children. In my own sarcoidosis material, which includes roughly 400 cases, I have observed but 4 cases below the age of 20—viz., in patients aged 19, 19, 18 and 15. For comparing the age distribution in sarcoidosis material with that in corresponding tuberculosis material I have selected female erythema nodosum cases of either type. The age distributions are presented in a diagram (Fig. 1) based exclusively upon patients aged 15 and older. As regards primary tuberculosis, it will be noted that the maximum incidence falls in the ten-year period following on puberty. It is, however, a well-known fact that primary tuberculosis with erythema nodosum—at least formerly—has been common also in children. Primary

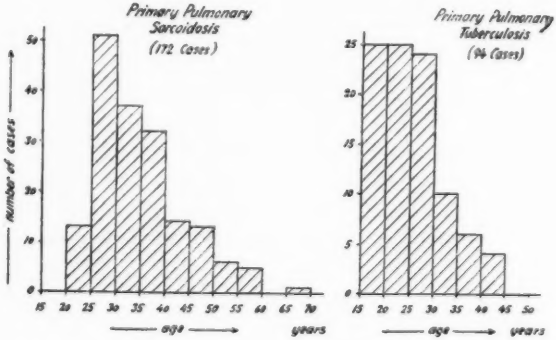

FIG. 1.—Comparison of age distribution in 172 cases of primary sarcoidosis and 94 cases of primary tuberculosis. All patients were women suffering from erythema nodosum.

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sarcoidosis with erythema nodosum, on the other hand, culminates between the ages of 25 and 30 years. Of cases below the age of 20 there are none at all in my series.

Sex

Lastly as to sex distribution. It is stated by most workers that there is a certain preponderance of the female sex in respect of the incidence of sarcoidosis. Now, it is of particular interest that primary sarcoidosis, when heralded by erythema nodosum, very often develops after childbirth. In no less than one-third of the 200 female erythema nodosum cases with primary sarcoidosis observed by me the erythematous eruption appeared during the period of lactation, mostly about six months after delivery, at the termination of suckling. To my knowledge such a relation is unknown in erythema nodosum associated with other infections.

Summary

Early pulmonary sarcoidosis is the commonest disease associated with erythema nodosum in Scandinavia today.

Primary sarcoidosis when heralded by erythema nodosum often develops within six months of the termination of pregnancy.

The blood uric acid level is often elevated in generalised sarcoidosis even when the non-protein nitrogen is normal or only slightly increased.

Hypercalcæmia has been observed in chronic sarcoidosis and a specific interstitial nephritis occurs in some of these.

Renal function is impaired in severe cases.

The frequency of sarcoidosis is subject to variations of climate and physiographical factors as well as in race, age and sex.

It is important to take notice of these variations when discussing the still obscure ætiology of the disease.

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AN EVALUATION OF THE CLINICAL SIGNIFICANCE OF CLUBBING IN COMMON LUNG DISORDERS

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Clubbing of the fingers and toes remains an unpredictable accompaniment of a variety of dissimilar lung diseases. Hypertrophic pulmonary osteoarthropathy, for instance, was noted by Wiermann, Claggett and McDonald (1954) in 5 per cent. of 481 instances of resected lung cancers, whereas Jack (1952) found only 3 cases of fully developed arthropathy in a series of 668 patients, Ray and Fisher (1953) observed 14 amongst 139 patients, and Ellman (1953) found 6 among 200 with lung cancer. The association of finger clubbing and bronchiectasis, according to Wiermann *et al.* (1954), was slightly more common with an incidence of 9·5 per cent. in 189 patients, whereas in a common lung disease like pulmonary tuberculosis, which in its chronic phase is so frequently associated with secondary bronchiectasis, the authors found one instance only amongst 157 tuberculous patients. In a review of 24 cases of lung cancer and arthropathy collected over seven years, Semple and McCluskie (1955) recorded one patient with clubbing and a metastatic lung tumour. A more common association is reported with such rare intrathoracic lesions as arteriovenous aneurysm of the lung (Adams, Thornton and Eichelberger, 1944; Barnes, Fatti and Pryce, 1948; Baker and Trounce, 1949) and fibroma of the visceral pleura (Price-Thomas and Drew, 1953). Mendlowitz (1942), however, listed bronchiectasis, lung abscess, empyema, protracted pulmonary tuberculosis, atelectasis, primary bronchial carcinoma, pleural fibroma, pulmonary hæmangioma, aortic aneurysm, cyanotic congenital heart disease, subacute bacterial endocarditis and bronchiectasis complicating mitral stenosis as the more common intrathoracic diseases in which clubbing may be, but is not necessarily, invariably seen. In addition clubbing may complicate non-pulmonary disorders such as myxœdema (Thomas, 1933), cirrhosis of the liver, ulcerative colitis, syringomyelia, Pancoast tumour involving the sympathetic ganglia (Mendlowitz, 1942); while unilateral clubbing and an axillary arteriovenous aneurysm on the same side was described by Cross and Wilson (1952). Finally, Camp and Scanlan (1948) recognised a group of patients, usually adolescent boys, with hypertrophic osteoarthropathy unaccompanied by any obvious primary disease which was regarded as again distinct from a hereditary form of clubbing in which the periosteal proliferation is never very extensive (1955, *Lancet*).

While Hippocrates in the fifth century B.C. described clubbing of the finger nails, von Bamberger (1889) and Pierre Marie (1890) related this physical sign to the presence of lung lesions. The present century has witnessed an

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extension of the clinical field of association to other diseases without, however, producing statistical evidence that such an association is necessarily significant, nor has the pathogenesis of clubbing thereby been illuminated. Semple and McCluskie (1955) have stressed the need for distinguishing clubbing without periosteal reaction and joint disability, as seen in chronic lung and congenital heart diseases, from arthropathy and clubbing, which appears as an infrequent early physical sign in patients developing a peripheral primary lung neoplasm (Craig, 1937; Rottjer, Aguilar and Lascalea, 1947; Temple and Jaspin, 1948; Wyburn Mason 1948; Pattison *et al.*, 1951; Hansen, 1952; Rasmussen, 1952; Ellman, 1953; Ray and Fisher, 1953; and Wiermann *et al.*, 1954).

Anatomical and Physiological Studies of Clubbed Fingers

Lovell (1950) examined the differences of the nail bed in patients with clubbing secondary to congenital cyanotic heart disease and that associated with lung disease, and noted that exsanguination of the fingers by elastic bandages altered the appearance and the tension in the nail bed of clubbed fingers with congenital heart disease, but not in other clubbed fingers. Blood volumes in the distal finger segments were greater in the congenital heart disease group only, but intra-arterial injections revealed an increase in fibrous tissue in all clubbed fingers, especially in the nail bed area. The specimens from congenital heart disease had, in addition, dilated skin venous plexuses in the nail bed area. A characteristic component was the increase in calibre of the digital arteries and the presence of local arteriovenous anastomoses in the distal finger segments near the junction of the dermis and the subcutaneous tissues with the efferent vessels opening into the deep venous plexuses in the distal phalanges. Lovell thought that the excess blood reaching the finger tips was largely directed through these anastomoses, and the by-pass of blood directly into the venous plexuses and away from the capillary bed might be responsible for the proliferative fibrous tissue changes seen in the terminal segments of clubbed fingers. This increase in local connective tissue was regarded as a result of an increase in blood flow which exceeded the local physiological needs, and its localisation to the distal finger segments is attributed to the predominance there of the arteriovenous anastomoses through which the increased flow is largely directed. This induces a state of chronic congestion and distension of the venous plexuses in the nail bed and skin with an excess in tissue fluid formation.

The local histological changes in the periosteum of fingers, forearm bones and synovial membrances of the joints in hypertrophic pulmonary osteoarthropathy were studied by Gall, Bennett and Bauer (1951), who demonstrated proliferative periostitis with lymphocytic and plasma cell infiltration and subperiosteal new bone formation.

Wilson (1952), studying local heat elimination from clubbed fingers under conditions of full vasodilation and after anæsthetising the ulnar nerve at the elbow, found that finger blood flow was increased. The flow could not, however, be further increased by eliminating nervous factors once full dilatation had taken place, and he thought it improbable that vasomotor nerves were responsible for the augmented peripheral blood flow in clubbing.

An Experimental Study

Mendlowitz (1938) observed that finger clubbing in certain lung and heart diseases was accompanied by arterial desaturation, an increased blood flow to the fingers, and a decrease in the pressure gradient in the brachial digital arterial tree. In 1941 the same author published an account of an experimental attempt at the production of clubbing in a dog. By anastomosing a pulmonary artery to the left auricle changes suggestive of pulmonary osteoarthropathy were produced. The main effect of this procedure was an augmentation of cardiac output and a reduction of the arterial oxygen saturation.

Observations

Brea (1948), Hansen (1952) and Flavell (1956) observed dramatic relief of joint symptoms following hilar neurectomy when lung resection was contra-indicated. Similarly relief of joint symptoms was accomplished by Wyburn Mason (1948) by tying the pulmonary artery on the side of the tumour. Subjective statements regarding the severity of joint pains and their subsequent relief are difficult to interpret, and as far as we are aware no objective measurements of grip improvement are available. The problem is even more complex in respect of objective measurements of finger volumes and blood flows after these procedures, but Semple and McCluskie (1955) mention that clubbing as well as joint pain and periostitis subsided after lung resection.

Fried (1943) reported 4 cases of bronchial neoplasm and osteoarthropathy; all four showed evidence of endocrine disturbances such as acromegalic facies, testicular atrophy, hirsutism, macroglossia and gynæcomastia, and suggest that clubbing might have an endocrine basis. Semple and McCluskie (1955) have not been able to confirm these endocrine findings in their series of 24 cases and were unable to recognise abnormalities in the pituitary, adrenal cortex and thyroid in three necropsies. Their biochemical investigations lent no support to an endocrine theory, and the dramatic response of the joint symptoms to surgery suggested a more direct effect between the neoplasm and the osteo-arthropathy.

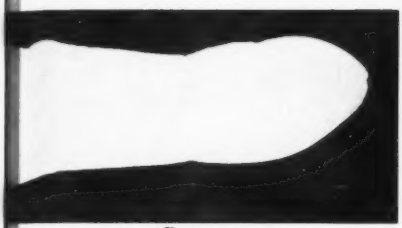
It emerges from these observations that an augmented peripheral flow alone appears to be a uniform finding in lung diseases complicated by clubbing. Yet diseases associated with an increase in cardiac output and peripheral blood flow such as thyrotoxicosis and Paget's disease (Edholm *et al.*, 1945) are seldom if ever complicated by clubbing of the fingers.

Clubbing and Anomalies: The Pulmonary Circulation

The possibility that an additional anomaly complicates those heart and lung diseases in which finger clubbing was a conspicuous feature prompted Cudkowicz and Armstrong (1953) to examine the bronchial circulation at post-mortem in a variety of these disorders. The study was carried out soon after death by means of a radio-opaque injection medium too coarse to penetrate vessels of less than 60μ in diameter, which was introduced into the bronchial circulation after careful removal of the total thoracic content. This method,

FIG. 1

A



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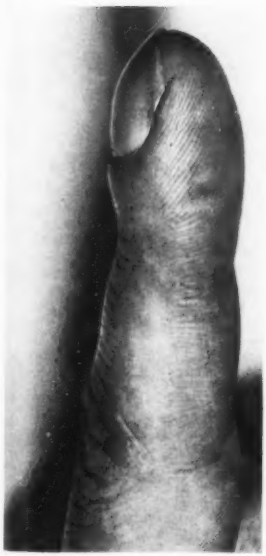
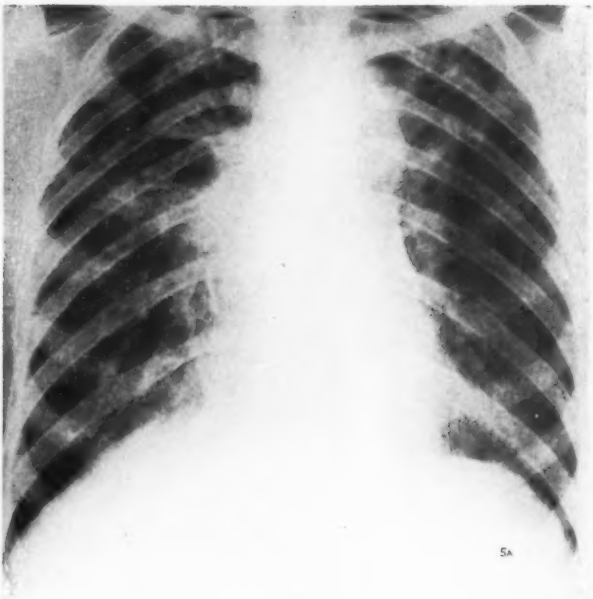


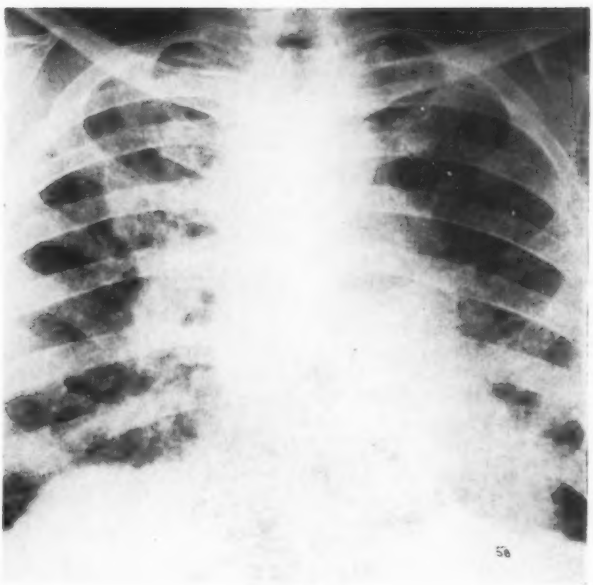
C

A — Silhouette of normal finger.
B — Silhouette of clubbed finger.
C — Photograph of B. A and B show difference in mass of terminal phalanx.

FIG. 5



A



B

A — Chest radiograph of Case 12. Sarcoidosis and drumstick finger clubbing.
B — Chest radiograph of Case 13. Sarcoidosis and normal fingers.

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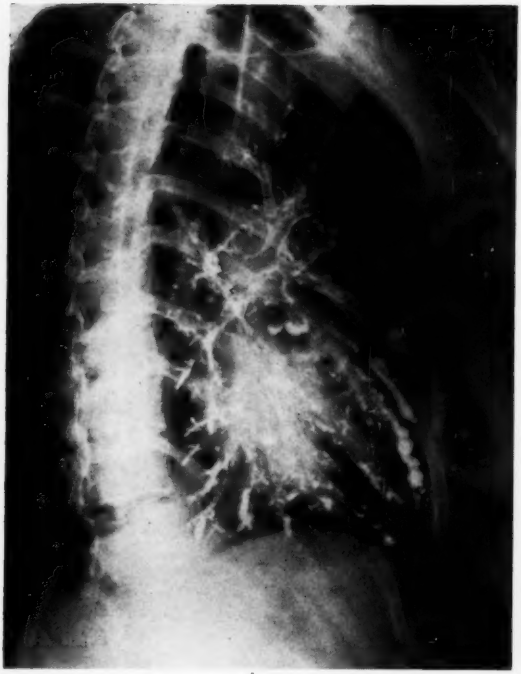
PLATE II

FIG 6



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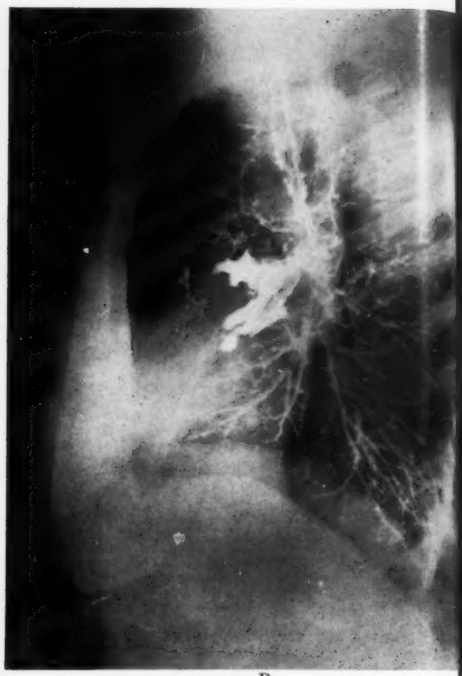

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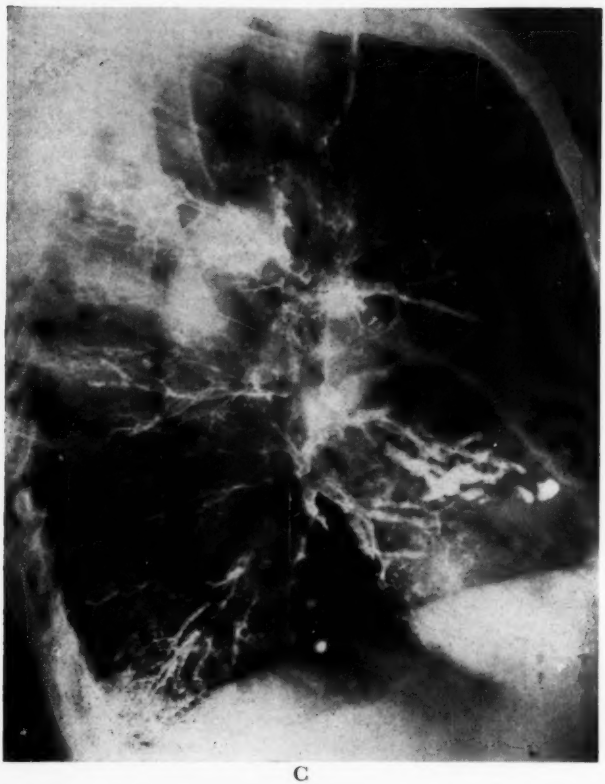

C

A — Case 17 (See table 1).

B — Female patient aged 32 with bronchiectasis of lingula, much sputum and normal fingers.

C — Case 28. Male patient aged 40 with right middle lobe bronchiectasis, no sputum and drumstick clubbing.

which was described in detail elsewhere (Cudkowicz and Armstrong, 1951), allows for both radiographic and histological examination of the bronchial and pulmonary circulations. The fixing properties of the injection medium permits in particular detailed microscopical identification of the injected vasculature in ordinarily stained lung sections. In sections in which the vessels have not been so injected, Brenner (1935), for instance, found the differentiation between bronchial and pulmonary arteries very difficult.

Cudkowicz and Armstrong (1953) examined the lungs of 15 subjects and in 12 of these both radiological and histological evidence of abnormal pre-capillary anastomoses between the bronchial and pulmonary arteries were found irrespective of the clinical diagnosis.

Nature of Pre-capillary Broncho-pulmonary Anastomoses

In all 12 cases at least one branch of the pulmonary artery showed partial occlusion of its lumen from thrombosis or medial sclerosis. Immediately beyond the occluded lumina, dilatation of the vasa vasorum in the adventitial coats of the pulmonary arteries became apparent. These arterioles, normally 100μ in diameter, are branches of the bronchial arteries (Miller, 1947; Cudkowicz and Armstrong, 1951). They penetrated the medial coats, which does not normally occur, and recanalised the occluded lumina, thus establishing a continuity between themselves and the patent peripheral pulmonary arteries. These anastomoses conveyed the injection medium, which was introduced into the bronchial arteries via the aorta, into the peripheral pulmonary arteries and also retrogradely into the proximal pulmonary arterial trunks, depending upon the degree of recanalisation that has taken place in that direction. No other types of anastomoses were seen. With the establishment of anastomoses via dilated vasa vasorum, the proximal bronchial arteries became considerably enlarged, whereas the smaller peripheral bronchial artery branches, which are normally extensively distributed throughout the whole lung and visceral pleura, showed very marked medial hypertrophy, and narrowing of their lumina, suggesting that they were in a state of reduced function.

Pre-capillary anastomoses between the two circulations are abnormal and there is no evidence that they occur in normal human lungs. (Miller, 1947; Cudkowicz and Armstrong, 1951). Wood and Miller (1938) obtained radiological evidence of pre-capillary broncho-pulmonary anastomoses in a variety of conditions, but the histological nature of these anastomoses or their possible relationship to clubbing was not emphasised. Liebow and colleagues (1949) demostrated broncho-pulmonary anastomoses in bronchiectatic lungs by means of a cast technique. Gilroy *et al.* (1951) found arterial blood in the pulmonary arteries of bronchiectatic lobes at operation prior to lobectomy and suggested that the increased oxygen saturation found was the result of bronchial arterial blood in the pulmonary arteries. In a more recent study of 14 cases of chronic lung disorders Roosenburg *et al.* (1954), using the cardiac catheter technique observed increased oxygen saturations in blood samples taken from single lung lobes.

Present Investigation

The clinical history, physical examination, chest radiographs including bronchography, electrocardiograms, hæmoglobin values, arterial oxygen-saturations, simple respiratory function tests such as the two second-time vital capacity and maximum breathing capacities, and simple right thumb volume estimates, have been recorded in 27 patients with drumstick clubbing who attended the Department of Thoracic Medicine, St. Thomas's Hospital, for a variety of respiratory ailments. These patients have also been studied by means of catheterisation of the branches of the pulmonary artery, but the results of this investigation will be recorded elsewhere. The purpose of this paper is the presentation of the clinical results obtained and a discussion of their relevance to the problem of clubbing in lung disease.

Measurement of Right Thumb Volume

The interpretation of clubbing of the fingers constitutes a problem in its own right (Pyke, 1954), and in order to avoid criticism of selection a definition of the degree of clubbing chosen seems necessary. In our view patients with drumstick clubbing show a marked expansion of the terminal phalanges of their fingers and toes. This expansion of the terminal phalanx volume approaching that of the intermediate phalanx is characteristic of well-developed clubbing and lends itself to measurement (see Plate, Fig. 1).

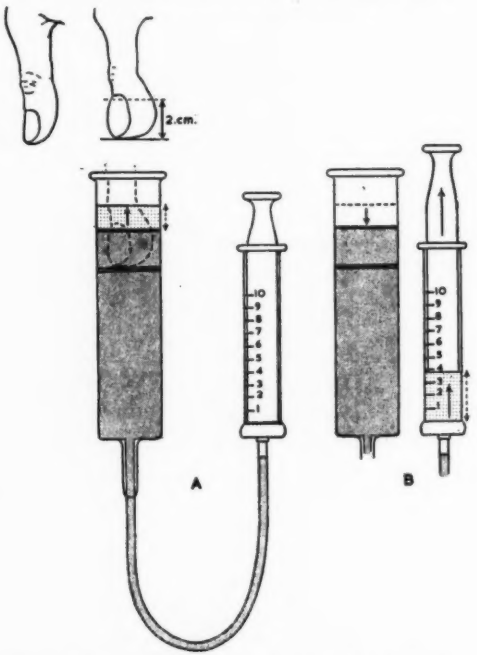

Fig. 2.—A perforated fixed platform in the left barrel limits the advance of the thumb, which displaces a 2 cm. high column of water.

TABLE A

No.	*Volume of R. thumb (terminal 2 cm.)*	*No.*	*Volume of R. thumb (terminal 2 cm.)*
1	6·25 ml.	15	6·0 ml.
2	6·5 ,,	16	5·5 ,,
3	9·0 ,,	17	5·25 ,,
4	5·75 ,,	18	4·75 ,,
5	8·0 ml. (before and after l. vagotomy)	19	6·0 ,,
		20	6·75 ,,
6	5·5 ml. (unchanged after hexamethonium)	21	5·5 ,,
		22	6·5 ,,
7	5·5 ml.	23	6·5 ,,
8	5·5 ,,	24	6·75 ,,
9	5·5 ,,	25	4·75 ,,
10	6·5 ,,	26	5·25 ,,
11	6·0 ,,	27	5·5 ,,
12	7·25 ,,	28	6·8 ,,
13	5·5 ,,	29	5·5 ,,
14	4·75 ,,	30	4·75 ,,

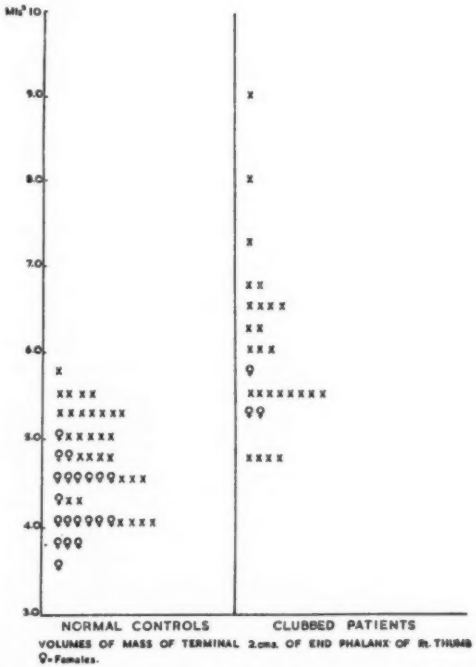

FIG. 3 shows that the volumes of mass of the terminal 2 cm. of the right thumb in 14 clubbed patients exceeded those in normals, and that the total figures for all the clubbed patients varied from 4·75 ml. to 9·0 ml. compared with those of 50 controls which ranged between 3·5 ml. to 5·75 ml.

The ventral slope of the terminal phalanx of the normal thumb diminishes the volume of that phalanx in comparison with the volume of the intermediate phalanx. The bulbous deformity of the clubbed thumb, however, renders this slope more convex and increases, in particular, the terminal 2 cm. mass of the terminal phalanx. By using a very simple water displacement method (see Fig. 2) the end 2 cm. of the fully extended thumb was measured and the figures of the clubbed patients were compared with those of 50 normal controls. The method gave reproducible readings from week to week and had an error not in excess of 0·5 ml.

Table A gives the figures of the right thumb measurements in the clubbed patients, and Fig. 3 compares these figures with those which obtained in 50 normal controls.

Material

The method of selection was in itself of interest inasmuch as drumstick clubbing was the only physical sign chosen to qualify for inclusion in this study. In that way a mixed number of disorders became assembled (Table 1) which at once suggested that clubbing was compatible with cyanosis, normal arterial oxygen saturations, hypopituitarism, and high as well as normal pulse pressures.

Similarly patients with bronchiectasis, whose only symptom was an occasional hæmoptysis, came under surveillance as well as those who expectorated profuse quantities of purulent sputum. One patient (13) without clubbing and suffering from sarcoidosis was included for control purposes, as the chest radiographs and clinical findings resembled those of case 12, a patient with sarcoidosis and gross finger clubbing (see Plate, Fig. 5). Two patients with doubtful clubbing have also been included for reasons of interest and control.

Results

Clubbing

The volume of the right thumb terminal phalanges of 24 patients with painless drumstick clubbing are shown in Table 1. In patients 5, 6 and 16 hypertrophic pulmonary osteoarthropathy with periosteal proliferative changes in the metacarpals and lower ends of their radii and ulnæ was demonstrated radiologically. Patient 16 suffered from severe bilateral bronchiectasis and patients 5 and 6 had primary peripheral bronchial cancers. The volume of the end 2 cm. mass of the left and right thumbs of patient 5 did not change following the division of the left vagus at the left hilum, although joint pains improved. Similarly no change in the volume of the right thumb was noted in patient 6 following a prolonged course of parenteral Hexamethonium.

Clinical History and Physical Examination of Lung Fields

The symptomatology in all patients was so variable that no one particular feature emerged which might have been indicative of a specific lung lesion. This applies in particular to hæmoptysis, quantities of sputum, cyanosis and breathlessness. Patients 6 and 14 presented with joint pains. The latter had a swollen and painful right wrist but failed to show periostitis radiologically.

Constant crepitations were audible in 14 patients in the area of one or more lobes, but apart from this other physical signs were inconstant and changed according to the temporary presence of bronchospasm and infection.

Respiratory Function Tests

Effort dyspnœa was a fairly common symptom and there appeared to be a reduction in volume of the two-second timed vital capacity in all patients (see Table 2). The maximum breathing capacity recorded over fifteen seconds showed much greater fluctuations and was within normal limits in 5 patients.

Radiology of the Lungs

Routine chest X-rays suggested a number of typical diagnoses such as carcinoma of the bronchus in 2, silicotic pneumoconiosis in 2, probable pneumoconiosis in 2, sarcoidosis in 4, probable arterio-venous aneurysm in 1, and pulmonary tuberculosis in 2 patients who had additional abnormalities elsewhere in the lungs. Six patients showed heterogeneous mottling and pleural fibrosis and had normal bronchograms. Their diagnoses remain obscure. Their respiratory function tests were grossly abnormal and suggested interstitial pulmonary fibrosis possibly as a result of past silent infarcts. In patients 27 and 29 emphysema was the only obvious radiological abnormality.

Bronchography aided with diagnosis in another 10 patients who showed variable degrees of bronchiectasis. (Plate, Fig. 6.) Patient 19 presented with an empyema in the right para-vertebral gutter twenty-three years after treatment for pulmonary tuberculosis. The right lower lobe showed areas of calcification with secondary bronchiectasis and the posterior basal bronchus of that lobe communicated with the pleural space.

Cardiovascular Findings

Central cyanosis was noted on a number of occasions in patients 4, 10, 12, 15, 16 and 26, particularly in the latter two. Twelve patients had a frank Corrigan quality of their peripheral arterial pulses and their pulse pressures exceeded 65 mm. Hg. In the remainder this physical sign was not present and pulse pressures were normal. Hypertension was absent in all patients.

Patients 12, 16, 23, 25, 26 and 29 had a right ventricular type of impulse palpable at the epigastrium. Pulmonary valve closure was palpable in patient 16.

Electrocardiograms

Patients 12 and 26 had large *p* waves and right axis deviation. Fourteen patients had small *r* waves in chest lead VI and patient 16 showed a frank right ventricular hypertrophy pattern. In 7 patients left axis deviation was recorded.

Hæmoglobin Values and Arterial Oxygen Saturations

As aforementioned, cyanosis was noted clinically in patients 16 and 26 in particular and the former had a hæmoglobin value of 17·6 g. per cent. with an arterial oxygen saturation of 89·4 per cent. High hæmoglobin values and arterial oxygen saturations under 90 per cent. occurred in 3 more patients. High hæmoglobin values and normal arterial oxygen saturation were also compatible and were seen in patients 10, 11, 13, 17 and 25 (see Fig. 4).

TABLE I

No.	*Age*	*Sex*	*Clinical diagnosis*	*Respiratory symptoms*	*Degree of clubbing*	*Volume R. thum (termin 2 cm.)*	
1	57	M	Idiopathic basal pulm. fibrosis	Dry cough and effort dyspnœa for 7 years	Drumstick	6·25 ml.	Rheu 194
2	53	M	Probable pneumoconiosis (dust exposure for 3 years æt. 17-20)	Effort dyspnœa since 1942 with cough and winter purulent sputum	,, ,,	6·5 ,,	Occas
3	59	M	Idiopathic basal pulm. fibrosis	Effort dyspnœa. Winter purulent sputum since 1951 fog	,, ,,	9·0 ,,	None
4	50	F	Pulmonary tuberculosis with large apical cavities	Cough and purulent sputum. Effort dyspnœa and episodes of cyanosis	,, ,,	5·75 ,,	Occas
5	56	M	Left upper lobe bronchial carcinoma	4/12 cough and mucoid sputum. Much weight loss	,, ,, +radiological periosteal thickening	8·0 ,, (before after L vagotom	Pain wrist inter
6	48	M	Left main bronchus carcinoma	Recent hæmoptysis, slight dyspnœa and much weight loss	Drumstick +radiological periosteal thickening	5·5 ml. (uncha after he methoni	/12 M.C wrist
7	55	M	Pneumoconiosis. Hypopituitarism. (Worked for 25 years with china-clay)	Progressive effort dyspnœa over 7 years	Drumstick	5·5 m	None
8	50	M	Pneumoconiosis. (Marble mason for 18 years)	Moderate effort dyspnœa over 2 years	,, ,,	5·5 ,,	,,
9	59	M	Pneumoconiosis. (In coal mines for 2 years)	Effort dyspnœa for 8 years. Cough and winter purulent sputum	,, ,,	5·5 ,,	Should
10	40	M	Sarcoidosis	Effort dyspnœa for 3 years	,, ,,	6·5 ,,	None
11	55	M	Sarcoidosis	Progressive effort dyspnœa for 6 years	,, ,,	6·0 ,,	,,
12	28	M	Sarcoidosis	Two hæmoptyses. Episodes of cyanosis. Dry cough. Effort dyspnœa	,, ,,	7·25 ,,	,,
13	46	M	Sarcoidosis	Effort dyspnœa for 3 years	,, ,,	5·5 ,,	,,
14	55	M	R.U.L. fibrosis and bronchiectasis	Nil	Drumstick R. hand	4·75 ,,	Pain a wrist
15	56	M	Widespread bilateral bronchiectasis	Cough. Very purulent sputum often 20 oz. daily for 4 years. Effort dyspnœa. Occasional cyanosis and ankle swelling	Drumstick +radiological periosteal thickening	6·0 ,,	None

Volume R. thum (termina 2 cm.)	*Joint symptoms*	*Physical signs in lungs*	*Chest radiographs*	*Bronchography*
6·25 ml.	Rheumatoid arthritis in 1949 arrested with gold	Crepitations in R.L.L.	Mottling of bases	
6·5 „	Occasional wrist pains	Crepitations R. and L.L.L.	Widespread reticulation	Normal.
9·0 „	None	Crepitations R. and L.L.L.	Mottling of bases	
5·75 „	Occasional arthralgia	Ronchi in both lungs	Large R. and L. apical cavities and infiltration and collapse of L.L.L.	2° bronchiectasis both R. and L.L.L. bronchi.
8·0 „ before a after L ragotom	Pain and swelling of wrists and proximal interphalangeal joints	Ronchi in both lungs	L. hilar shadow and L. mid-zone opacity	
5·5 ml. unchan after he ethoni	8/12 pain and swelling M.C.P. and ankles and wrists	P.N. ↓ L.U.L.	Shadows in L.U.L., L. hilum and 2° in R.L.L.	
5·5 ml	None	None	Bilateral reticulation	
5·5 „	„	Few crepitations R. and L.L.L.	„ „	Normal.
5·5 „	Shoulder pains	Few crepitations R. and L.L.L.	L. hilum enlarged and fine bilateral reticulation	„
6·5 „	None	None	Both hila enlarged. Bilateral reticulation R.U.L., fibrosis and elevation of R. diaphragm	„
6·0 „	„	Crepitations R. and L.L.L.	Bilateral diffuse reticulation	„
7·25 „	„	Crepitations R. and L.L.L.	Basal fibrosis. R.M.L. honeycombing. Widespread reticulation	„
5·5 „	„	Crepitations in mid-zones	R. hilum enlarged with bilateral reticulation	„
4·75 „	Pain and swelling of R. wrist	Percussion note ↓ with rhonchi in R.U.L.	Fibrosis and retraction of R.U.L. with small bulla	Cystic dilatation of apical and posterior bronchi R.U.L.
6·0 „	None	Widespread crepitations	Cystic changes and mottling of both lungs	Bilateral extensive ectasia.

TABLE I (*continued*)

No.	*Age*	*Sex*	*Clinical diagnosis*	*Respiratory symptoms*	*Degree of clubbing*	*Volume R. thu... (termi... 2 cm.*
16	31	M	Bilateral lower lobe bronchiectasis	Cough and winter sputum since birth. Progressive effort dyspnœa and frequent bouts of cyanosis and dyspnœa at rest and ankle swelling	Drumstick	5·5
17	26	F	Bronchiectasis of lingula	5-year cough with occasional winter purulent sputum	" "	5·25
18	48	M	Bronchiectasis of left lower lobe and lingula	Dry cough. Occasional winter purulent sputum	" "	4·75
19	48	M	Old healed calcified tuberculosis of R.L.L. with recent bronchopleural fistula at R. base posteriorly	Hæmoptysis, purulent sputum, empyema in last 5/12	Moderate clubbing	6·0
20	66	M	Bronchiectasis of part of L.L.L. and lingula	Cough all his life with 1-1½ oz. of purulent sputum daily. One hæmoptysis	Drumstick	6·75
21	66	M	Apical fibrosis and basal emphysema	Effort dyspnœa with cough and occasional winter purulent sputum	" "	5·5
22	60	M	Apical fibro-caseous tuberculosis and R.L.L. fibrosis	Effort dyspnœa with cough and recent purulent sputum	" "	6·5
23	46	M	Emphysema of R. mid. and lower lobe and left basal fibrosis	Cough since childhood with 2-3 oz. purulent sputum daily	" "	6·5
24	63	M	Idiopathic pulmonary fibrosis	11 years of progressive effort dyspnœa. Also cough and regular winter purulent sputum	" "	6·75
25	50	M	Idiopathic pulmonary fibrosis	Dry cough with progressive dyspnœa of insidious onset	" "	4·75
26	45	F	Idiopathic pulmonary fibrosis +cor pulmonale	Progressive dyspnœa, dry cough and frequent bouts of cyanosis and swelling of ankles and calves	" "	5·25
27	51	M	" Emphysema "	Dry cough. Effort dyspnœa and occasional ankle swelling	" "	5·5
28	46	M	2° bronchiectasis and atelectasis of R.M.L.	Dry cough since 15. One hæmoptysis	" "	6·8
29	53	M	" Emphysema "	Effort dyspnœa with dry cough	" "	5·5
30	42	M	?Arterio-venous aneurysm of L.L.L.	Recent hæmoptysis	Moderate clubbing	4·75

Volume R. thu (term 2 cm.	*Joint symptoms*	*Physical signs in lungs*	*Chest radiographs*	*Bronchography*
5·5	ne	Crepitations R. and L.L.L.	Mottling with cystic changes in lower lobes	Ectasia of R.L.L., L.L.L. and lingular bronchi.
5·25		Crepitations L. axilla and L.L.L.	Mottling in L.L.L.	Lingular bronchiectasis.
4·75		Percussion note ↓ L.L.L.	,, ,, ,,	Bronchiectasis of L.L.L. and lingula.
6·0		Percussion note ↓ R.L.L.	Retraction of R. hilum. Calcification in R.L.L. R. basal pleural shadowing	2° ectasia lateral and post. basal bronchi R.L.L. The latter communicated with pleural space.
6·75	ins and needles" in nger tips	None	Mottling at L.L.L. with some emphysema of L.L.L.	Bronchiectasis of lingula and anterior basal bronchiectasis L.L.L.
5·5	ne	Percussion note ↓ apices	Bilateral apical fibrosis. Emphysema of lower lobes	Bronchiectasis of R.U.L. and lingula.
6·5		None	R. apical and L.U.L. infiltration and fibrosis of R.L.L.	Not attempted.
6·5		Crepitations and rhonchi in both upper zones	Fibrosis of apices and bases and mid-zone emphysema	,, ,,
6·75		Crepitations in R. R. and L.L.L.	Fibrosis of mid-zones and R. apex	Normal.
4·75		None	Fibrosis of all zones and elevation of hila and diaphragm	,,
5·25		,,	Emphysema. Large pulmonary arteries. Old healed tuberculosis L. hilum	Distortion only of L. main bronchus.
5·5		,,	Emphysema	Normal.
6·8		Crepitations R.L.L.	Atelectasis of R.M.L.	2° bronchiectasis of R.M.L.
5·5		None	Emphysema	Normal.
4·75		Bruit in L.L.L.	Vascular shadow in L.L.L.	Not attempted.

TABLE II

No.	*C.V.S.*	*B.P.*	*Pulse pressure*	*E.C.G.*	*Hb. (g.)*
1	Normal	170/85	85	L.A.D.	15·3
2	„	130/80	50	Vertical heart. Small R. wave V.1	13·1
3	„	185/80	105	R.A.D.	16·2
4	„	150/80	70	„	13·6
5	„	190/100	90	Normal	13·2
6	„	125/85	40	„	10·3
7	„	140/65	75	Small R. wave V.1	15·1
8	„	140/80	60	„ „ „	16·5
9	Short apical systolic murmur	160/80	80	L.A.D. T. wave inverted L.3	16·8
10	„	145/85	60	R.A.D. with small R. wave in V.1	17·02
11	„	160/100	60	R.A.D. with small R. wave in V.1	17·46
12	R. ventricular impulse P2++	120/90	30	R.A.D. big P. waves in L.2 and A.V.F. R. wave in V.1	18·35
13	Normal	135/85	50	L.A.D.	17·46
14	„	145/65	80	Small R. wave in V.1	15·15
15	„	120/80	40	„ „ „	17·1
16	R. ventricular impulse+. Pulm. valve closure impulse. Proto-diastolic triple rhythm	100/80	20	R.V.+vertical heart and big P. waves	17·6
17	Normal	125/65	60	Vertical heart	14·35
18	„	125/60	65	Small R. in V.1	15·1
19	Short apical systolic murmur	135/85	50	L.A.D.	16·6
20	Normal	145/75	70	„	14·7
21	„	115/60	55	R.A.D. small R. wave in V.1	11·5
22	„	140/75	65	L.A.D.	15·0
23	Apex displaced. R. ventricular impulse	120/80	40	Vertical heart	16·3
24	Normal	145/80	65	L.A.D.	18·3
25	R. ventricular impulse	150/80	70	R.A.D. R. wave in V.1	18·15
26	„ „ „	125/55	70	R.A.D. small R. wave in V.1	15·8
27	„ „ „	140/90	50	P. pulmonale. Small R. wave in V.1	13·6
28	Normal	140/90	50	P. pulmonale. Small R. wave in V.1	17·1
29	R. ventricular impulse+. Proto-diastolic gallop	190/90	100	Vertical heart with small R. wave V.1	14·7
30	Normal	155/65	90	Normal	10·5

Arterial O_2 saturation (per cent.)	*2-second timed vital capacity (ml.)*	*Maximum breathing capacity in l. per m.*	*Miscellaneous*
Not available	2905	86·300	
" "	2802	43·500	
" "	1743	105·900	
" "	Not available	Not available	
94·4	" "	" "	L. pulmonary artery saturation (specimen taken at operation for L. vagotomy) = 78·23%.
92·1	" "	" "	
93·8	1893	48·460	Patient only shaves thrice weekly. Has feminine distrib. of hair. Pituitary X-ray normal. 17 ketosteroids in urine = 10·3 mg.
90·9	1864	36·520	
Not available	1140	44·144	
92·0	1704	58·080	
91·6	2116	53·744	
89·45	2235	99·200	
96·6	2407	113·212	
97·6	1992	59·380	
87·5	1370	44·08	
89·4			
94·4	1204	42·330	
98·4	1820	80·340	
94·3	2448	48·770	O_2 saturation in pul. artery branch at operation = 92·0%.
96·5	2792	101·240	
Not available	1660	60·4	Patient died and histology of R.U.L. showed no evidence of Tb. Vasa vasorum were seen in communication with pulmonary arteries which also showed intimal hyperplasia.
94·3	2075	113·544	
90·8	1936	58·392	
90·1	2075	30·956	
93·4	1443	39·700	
89·4	1325	36·425	
94·3			
Not available	1950	87·600	
" "	1990	50·000	
96·45			

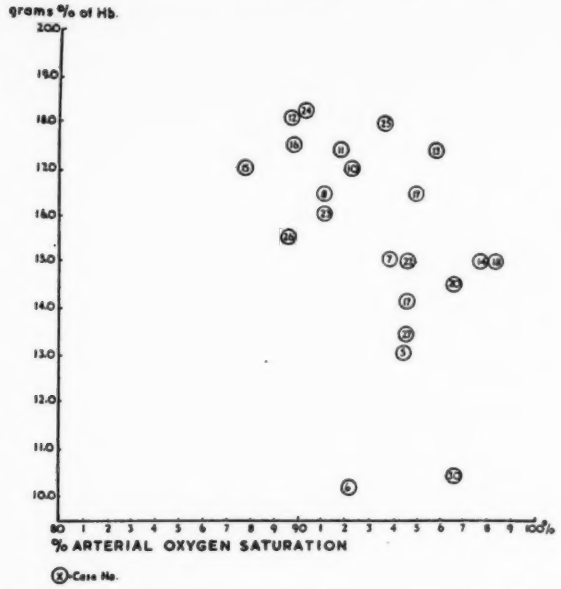

FIG. 4.—Arterial oxygen saturations and hæmoglobin values in 22 patients.

Changes in the Pulmonary Circulation

In 4 patients of the 24 in this series who have been studied by cardiac catheterisation pulmonary hypertension was present. In cases 15, 16 and 27 this was associated with bilateral pre-capillary broncho-pulmonary anastomoses. This rise in pressure was not associated with either anoxia or heart failure at the time of the examination. The arterial oxygen saturations were 87·5, 89·4 and 94·3 per cent. respectively, while the oxygen saturations in two lobar branches of the pulmonary artery exceeded those of both the right ventricle and the main pulmonary artery respectively. Details of this study have been separately compiled (Cudkowicz and Wraith, 1956).

Discussion

Analysis of the clinical findings in this series of 27 patients with finger clubbing has failed to yield a common clinical denominator which might illuminate this association with the lung disorders studied. This applies to age, clinical history and physical signs in the lung fields. The sex incidence appears to favour males. Both infection and its absence are compatible with clubbing, as well as normal and decreased arterial oxygen saturations. Neither the radiology of the chest nor bronchography have shown constant abnormalities apart from features characteristic of the individual lung diseases.

The cardiovascular, electrocardiographic and pulse-pressure findings were equally variable, but absence of hypertension and frequently raised hæmoglobin values which were not related to lowered arterial oxygen saturations may be of significance.

Ventilatory function tests in respect of two-second timed vital capacity and maximum breathing capacity were not helpful. Carbon monoxide diffusion studies could, unfortunately, not be carried out, but it is unlikely that a small peripheral neoplasm would significantly influence carbon monoxide uptake.

Left hilar neurectomy and a ganglion blocking agent such as hexamethonium bromide did not alter the shape or volume of the thumbs in 2 patients with hypertrophic pulmonary osteoarthropathy.

Even this small series of patients suggests, therefore, that clubbing is related to an added abnormality which occasionally complicates lung diseases, and that the elucidation of this anomaly requires methods other than simple clinical tests. This anomaly is probably localised to the pulmonary circulation, because clubbing disappears after excision of small lung tumours and of arterio-venous aneurysms of the lung (Semple and McCluskie, 1955).

The tumour itself is unlikely to be directly related to finger clubbing, as the majority of lung cancers do not become so complicated. Wiermann *et al.* (1954) noted an incidence of only 5 per cent amongst 481 resected lung cancers. Abnormal broncho-pulmonary precapillary anastomoses near the growing tumour have, however, been noted near lung cancers associated with painful clubbing (Cudkowicz and Armstrong, 1953) and it must be presumed that these localised vascular anomalies are also excised with the resection of the lung tumour, in which case it is reasonable to assume that the disappearance of the clubbing is as much attributable to the removal of the vascular abnormality as to excision of the cancer, particularly since the ablation of the vascular anomaly in arterio-venous aneurysm of the lung has the same effect.

Finger clubbing in lung disease points, therefore, to the existence *in vivo* of the same abnormal communications between the bronchial and pulmonary arteries in at least one lung lobe which was noted in post-mortem studies of similar diseases (Cudkowicz and Armstrong, 1953). In a separate study the results of catheterisation of the lobar branches of the pulmonary arteries of 24 of the present series of patients have been recorded (Cudkowicz and Wraith, 1956). In 16 patients significantly raised arterial oxygen saturations in at least one lobar branch of abnormal lobes were noted, and in 3 cases this abnormality was present in at least two lobes. The latter patients had raised pulmonary artery pressures without suffering from heart failure or anoxia. The rise in pulmonary artery pressure is of interest inasmuch as it can be related to bilateral broncho-pulmonary anastomoses rather than functional hypotheses of anoxia or heart failure (von Euler and Liljestrand, 1946, Mounsey *et al.*, 1952). While anoxia produces slight elevations in pulmonary artery pressure (Nahas *et al.*, 1954; Fishman *et al.*, 1955; and Bühlmann and Hossli, 1956), this rise is transitory and complicated by a disproportionate rise in cardiac output. In patent ductus arteriosus pulmonary artery pressure remains normal for long periods in spite of augmented pulmonary blood flow, but it often rises to a considerable extent later in the presence of raised arterial oxygen saturations in the pulmonary arteries (Harris, 1955) before flow reverses through the ductus, and presumably as a result of structural changes in the smaller pulmonary arteries (Gilmour and Evans, 1946). Occlusive changes in the smaller pulmonary arteries are a mechanism which initiates the formation of

broncho-pulmonary anastomoses, and their establishment on a wide enough scale in our 3 cases was associated with both clubbing and raised pulmonary artery pressures.

If precapillary broncho-pulmonary anastomoses are the common factor shared by lung lesions and finger clubbing, a somewhat similar anomaly (between hepatic arteries and portal veins), obtains occasionally in cirrhosis of the liver, which is also known to have this infrequent association (Dock, 1947).

The mechanism whereby broncho-pulmonary pre-capillary anastomoses influence the genesis of clubbing remains a matter of conjecture until further fundamental knowledge accrues in respect of the pulmonary and bronchial circulations as well as of the organisation of the afferent nervous pathway from the parenchyma of the human lungs and its central cord connections. Division of the vagus at the hilum of one lung has in our experience not influenced the degree of finger clubbing and is unlikely to do so in view of the bilateral innervation of each lung. Intra-pulmonary nerve ganglia depend for their blood supply on the vasa-nervosa of the bronchial arteries and, provided that this circulation and one nervous pathway remains intact, afferent impulses from the lung periphery will continue to reach the central nervous system.

Summary

Clubbing of the fingers is an infrequent association of common lung diseases. Its incidence in lung cancers, for instance, is about 5 per cent and less than 0·2 per cent, in pulmonary tuberculosis. While anatomical studies of the affected fingers show a fairly uniform abnormality, no equivalent single abnormality can be clinically found in either the lung fields or cardiovascular system. In an analysis of 27 patients with drumstick clubbing not one single clinical factor emerged which was common to all patients. This applied in particular to age, sex, history, physical signs in lungs and heart, pulse pressure, chest-radiograph, bronchography, electrocardiogram, ventilatory function test, hæmoglobin values and arterial oxygen saturations. No relationship between arterial oxygen desaturation and hæmoglobin values could be established. Hypertension was, however, absent in all patients.

A ganglion blocking agent and unilateral hilar neurectomy had no effect on the shape and volume of the clubbed thumbs of 2 patients.

This absence of a common clinical denominator points to the presence of an additional anomaly, probably in the pulmonary circulation, which requires for its demonstration such methods as catheterisation of the lobar branches of the pulmonary arteries. The nature of this anomaly is thought to be the formation of pre-capillary broncho-pulmonary anastomoses in abnormal lobes. Bilateral pre-capillary broncho-pulmonary anastomoses in 3 patients of this series were associated with pulmonary hypertension. The nature of these anastomoses and their possible relationship to finger clubbing has been discussed.

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SKIN LESIONS IN DISEASES OF THE CHEST

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In this paper it is intended to outline the cutaneous manifestations of tuberculosis, sarcoidosis and polyarteritis nodosa.

Tuberculosis

Tuberculosis of the skin occurs in a variety of forms which carry separate names. Some of these conditions are always due to tuberculosis, some are due to tuberculosis or some other condition, whilst the remainder are believed to be due to tuberculosis, but the evidence on which this belief is based is far from complete. In the first group is lupus vulgaris, in the second erythema nodosum and in the third acne agminata (lupus miliaris disseminatus faciei).

For descriptive purposes cutaneous tuberculosis is best divided into two main divisions: those in which tubercle bacilli are present in the lesions and those in which tubercle bacilli cannot be found in the lesions, but the cutaneous reaction is due to tuberculosis elsewhere in the body. Each of these divisions is further subdivided into primary tuberculosis and later stages of the disease. These are shown in Table I.

Table I.—Classification of Cutaneous Tuberculosis

Bacilli present in the Lesions	*Bacilli not present in the Lesions: reaction secondary to disease elsewhere*
Primary tuberculosis of the skin (tuberculous chancre)	Erythema nodosum
Miliary tuberculosis	Erythematous tuberculide
	Erythema induratum (Bazin)
Lupus vulgaris	Papulo-necrotic tuberculide
Tuberculosis verrucosa cutis	Lichenoid tuberculides (including lichen scrofulosorum)
Scrofuloderma	Lupus miliaris disseminatus faciei (acne agminata; acnitis)
Tuberculosis cutis orificialis	Rosaceous tuberculide (micropapular tuberculide)

Primary tuberculosis of the skin is uncommon but presents a characteristic picture. It usually occurs in children on the exposed parts of the body. A small nodule forms at the site of inoculation, which quickly develops the characteristic yellow colour seen in the nodules of lupus vulgaris when viewed through a glass slide pressed gently on the lesion. The nodule tends to change into a depression, which may ulcerate; the adjacent lymph node becomes enlarged and may be tender. This node is one which is not commonly enlarged in other conditions. Thus a primary tuberculous lesion on the cheek or lower eyelid will be accompanied by enlargement of the preauricular node on the same side. Primary tuberculosis of the skin normally clears entirely. The

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FIG. 1.—Lupus Vulgaris.

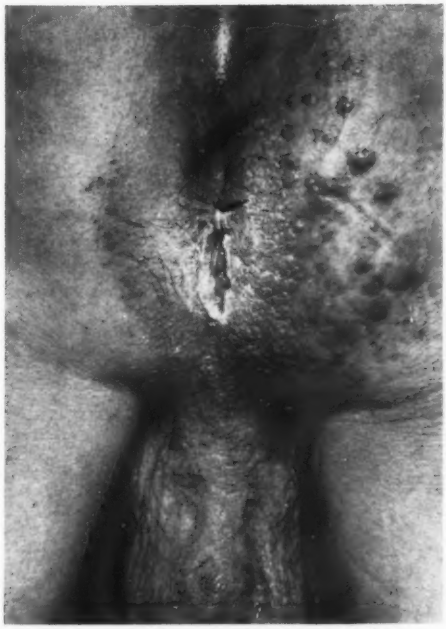

FIG. 3.—Tuberculosis cutis orificialis.

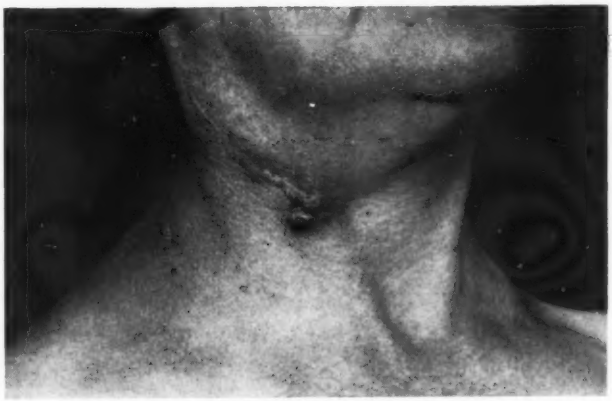

FIG. 2.—Scrofuloderma.

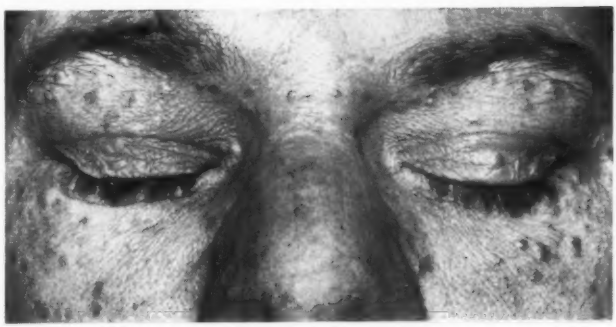

FIG. 4.—Lupus miliaris disseminatus faciei.

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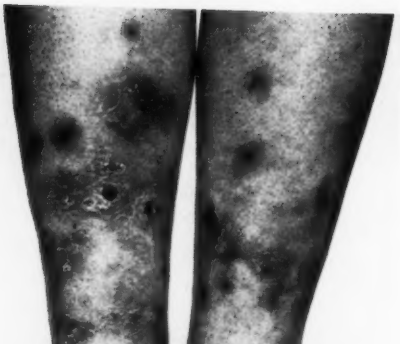

FIG. 5.—Bazin's disease.

FIG. 6.—Boeck's sarcoid of cheek; plaque type.

FIG. 7.—Sarcoid infiltration of toes.

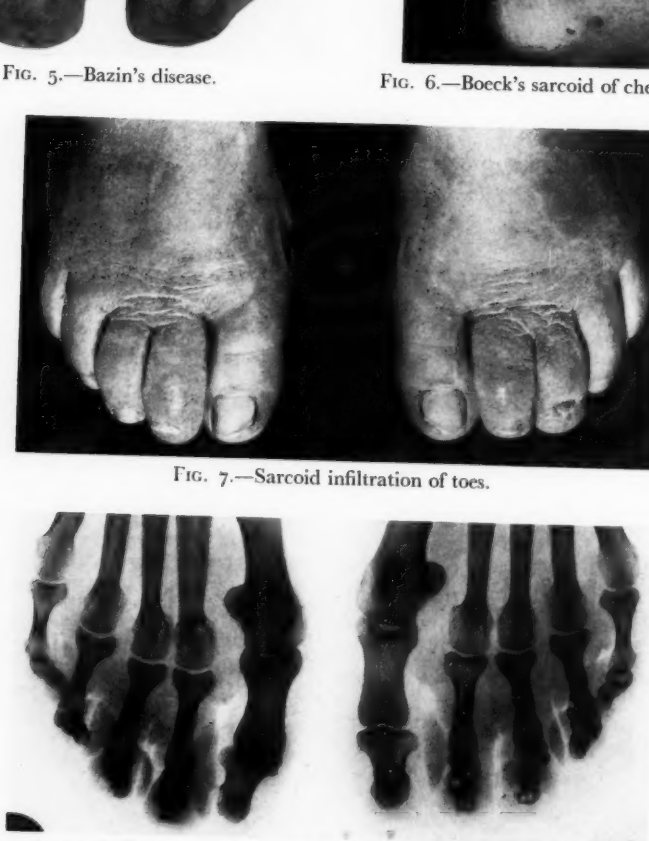

FIG. 8.—Same patient as in Fig. 7, showing sarcoid infiltration of terminal phalanx of left middle toe.

nodule may, however, increase in size and develop into lupus vulgaris, the lymph node subsiding, or the skin lesion may clear and other evidence of the disease appear elsewhere in the body. Until there is evidence of progression, active treatment is best witheld. The Mantoux reaction, at first negative, becomes positive after a few weeks.

Miliary tuberculosis of the skin is now seen more often than in the past owing to the greater length of survival of these patients. The lesions are very varied and consist of small macules, papules, vesicles or purpuric lesions. No special treatment is required for the skin lesions.

Lupus vulgaris is the commonest form of cutaneous tuberculosis. Treatment is now so satisfactory that the extensive scarring seen in the past need not occur. The condition may start as a progression from the lesion of primary skin tuberculosis or as an extension from scrofuloderma, but usually it arises from inoculation of tubercle bacilli into the skin of patients from outside the body and who have had their primary lesion elsewhere. At the start there is a small nodule which increases in size very slowly with a tendency to clear in the centre with scarring. The usual site is the face (see Fig. 1), and the nose or the ear lobes are frequently involved. On diascopy, the characteristic yellow ("apple jelly") nodules are seen. Histologically, the condition is typically tubercular but without caseation. Tubercle bacilli can be recovered on animal inoculation but can seldom be found otherwise; they are either of human or bovine type. Treatment is remarkably successful. Until quite recently ultra-violet light alone from the Finsen lamp was used with great success, but the introduction of the use of calciferol by Dowling and Prosser Thomas (1945) in this country and Charpy (1944) in France was a great advance and much reduced the time and difficulties in treatment. Many cases which had failed to respond to ultra-violet light were cleared with calciferol. More recently isonicotinic acid hydrazide has been used alone or in combination with calciferol or streptomycin, with even greater success and fewer side effects. The ease of resolution of lupus vulgaris has led to the belief that tubercle bacilli in the skin become less virulent than when present elsewhere in the body and there is some evidence that this is true (Dowling and Wetherley-Mein). Calciferol is given in tablet form 150,000 units daily for two or three months and reducing to 100,000 units daily or as an alcoholic solution (Sterogyl-15 ampoules) 400,000 units twice a week reducing to once a week. The usual dose of INAH is 100 mg. three times a day (3-8 mg. per kilo body weight). Calciferol is contra-indicated if chest lesions are present. There are important toxic effects from calciferol and they are due, in most cases, to an elevation of blood calcium leading to kidney damage. Toxic symptoms begin with a feeling of well-being followed by thirst, anorexia, sickness and lassitude. Unfortunately kidney damage can occur without any warning symptoms, so it is well to keep a record of blood calcium levels in all patients and to investigate further if there is any significant rise.

The extensive scarring and deformities seen in the past from lupus vulgaris need not occur with modern methods of treatment. Epitheliomata developing on lupus scarring is still seen, but usually in patients who have had X-ray treatment many years previously. There is now no place for X-ray therapy for lupus vulgaris.

Tuberculosis verrucosa cutis or warty lupus is in all respects similar to lupus vulgaris except that it tends to start later in life and is always the result of inoculation of tubercle bacilli into the skin from outside the body. There is much overgrowth of epidermis and especially the horny layer. This gives the warty appearance. Here again either the human or bovine type of tubercle bacillus is responsible, the bovine bacillus being responsible in the type known as the butcher's wart. Histologically the picture is much less clear-cut than in lupus. The condition responds well to treatment with calciferol and INAH.

In scrofuloderma the tubercle bacilli usually enter the skin from a breaking-down gland or from extension of a tubercular infection in bone or joint, but there is a small group of cases where it results from blood-stream dissemination following an acute febrile illness, usually measles (Fig. 2). In these cases there are multiple foci of infection in the skin, but they are now very rare. It is perhaps better to regard such cases as disseminate lupus vulgaris. The commonest site for scrofuloderma is the neck and it usually follows operation for removal of tubercular glands. Tubercle bacilli are more plentiful than in lupus. The condition readily responds to modern forms of treatment. In the past the condition might progress in the skin and become indistinguishable from lupus.

Tuberculosis cutis orificialis (Fig. 3), as its name suggests, occurs around the orifices, usually mouth or anus. It is due to direct implantation of bacilli in relation to active disease in chest or gut. The name is used to include tubercular ulcers in the mouth and on the tongue and also the mucous membrane of the rectum. These ulcers are deep and painful and respond only slowly to treatment. The lesions in the skin look like lupus and clear quickly when treatment is instituted. The condition is only an incident in the course of a more serious disease.

Erythema nodosum is the most important cutaneous manifestation of tuberculosis which occurs without evidence of tubercle bacilli in the lesions, but secondary to disease elsewhere in the body. It is, however, by no means always due to tuberculosis. It may be described as a condition which occurs in association with a mild febrile illness in most cases. The eruption appears suddenly as shiny tender nodules on the front of the shins, at first pink in colour and in various sizes from a few millimetres to 2-5 centimetres across. In the first few days they may coalesce to form a large erythematous area, but this quickly begins to subside and the individual lesions are again easily distinguished. The colour may remain pink, but often changes through blue to brown as in a bruise. The tenderness subsides and the lesions fade in two to three weeks. Lesions may occur elsewhere on the body, but almost always the shins are involved.

The cause of erythema nodosum is considered by most authors to be a non-specific manifestation of hypersensitivity to various allergens, mainly bacterial. The causative agent varies according to age and country. In Britain, primary tuberculosis is the cause in the majority of childhood cases (about 70 per cent.) (Doxiadis, 1949; Perry, 1944) and in about a third of adult cases. Streptococcal throat infection accounts for the majority of the remainder. In Scandinavia the tubercle bacillus is responsible for almost all the childhood cases (Wallgren, 1938) and for about 50 per cent. of adult cases (Löfgren, 1946), although in some of these it appears to be due to the tubercle bacillus in the later stages of

the disease. Looked at the other way, what proportion of cases of primary tuberculosis show erythema nodosum? The figures vary widely and are probably unreliable. In Scandinavia the number is given as 5 to 10 per cent. in children, but 30 per cent. if other evidence of tubercular infection is present (Meyer, 1949). Marc Daniels (1944) showed in this country that only 5 of 285 nurses on Mantoux convertion developed erythema nodosum.

In the San Joaquin valley of California "valley fever," as the disease is known locally, is almost always due to infection with coccidioides immitis, a deep fungus infection (see Thorner, 1939, for literature relating to this condition). The picture of erythema nodosum is also not uncommonly seen following treatment with sulphonamides and various attempts have been made to explain this. It seems probable that the drugs themselves and some other drugs may occasionally be responsible, but in other cases it may be due to the infection for which the drug was given or to a resurgence of tuberculin sensitivity following temporary depression produced by some intercurrent infection. The rare recurrences of erythema nodosum probably come into this last group of cases.

Erythema nodosum is not infrequently associated with hilar gland enlargement, as might be expected with primary tuberculosis, but in some cases there is bilateral hilar gland enlargement and a negative Mantoux reaction. This has led some writers to say that on occasions erythema nodosum may be a disease in its own right. There is a growing belief, however, that these cases are really manifestations of sarcoidosis and, in some, extensive mottling of the lung fields confirms this belief (Kerley, 1943).

The histology is the same in all cases: a perivascular infiltrate of polymorphonuclear leucocytes and lymphocytes in the lower part of the cutis and in the subcutaneous tissues. There may be endothelial proliferation of the blood-vessel walls which at times leads to thrombosis. There may be fat necrosis.

TABLE II.—CONDITIONS PRODUCING THE PICTURE OF ERYTHEMA NODOSUM

1. Primary tuberculosis
2. Streptococcal infections
3. Other infections, including coccidioides immitis
4. Drugs, especially sulphonamides
5. Sarcoidosis

The erythematous tuberculide was described by Hohmann but is not well recognised. It is a fleeting condition which occurs at a time when tuberculin sensitivity has developed and reached a very high level.

The remaining tuberculides all occur in the later stages of tuberculosis. Erythema induratum or Bazin's disease is the name given to a nodular condition occurring on the legs in young women (Fig. 5). The condition is comparatively uncommon and the lesions appear on the backs of the calves and consist of recurring indurated nodules, which persist for months or years and from time to time ulcerate, forming rather deep indolent ulcers. The patients are otherwise quite fit and there is little or no evidence of active tuberculosis elsewhere in most cases, though a history of tuberculosis can be elicited. The histology is frankly tubercular with caseation, but there is also an important vascular element present consisting of periarteritis, endarteritis and phlebitis affecting

arterioles and venules and some larger vessels. This leads to necrosis of fat and extensive fibrosis which in the later stages may obscure the tuberculoid structure.

There are other causes of nodules of the legs and these greatly outnumber the cases of true Bazin's disease, and some people now believe that Bazin's disease does not exist as an entity (Lynn, 1954). Dermatologists are unwilling to accept this view. The other main causes of indurated nodules on the legs are given in Table III.

TABLE III.—CONDITIONS PRODUCING THE PICTURE OF ERYTHEMA INDURATUM

1. Bazin's disease
2. Erythema induratum of Whitfield
3. Perniosis
4. Trichophyton rubrum infection

In infection with trichophyton rubrum the fungus may spread into the hair follicles and the lanugo hairs in the area will be found to contain the fungus.

Papulo-necrotic tuberculides occur during the course of active tuberculosis as small pustules or papules which ulcerate and then heal with depressed scars. They are most common on the limbs, but may occur on the face or trunk. They occur in crops and tend to be rather painful. The patient, although he has active tuberculosis, is usually not very ill. The histology is rather characteristic. There is a small central necrotic area surrounded by a typical tubercular focus and it is often perifollicular in position. The individual lesions are seldom more than 1-2 mm. across.

Lichen scrofulosorum is now seldom seen. It was a disease chiefly of children and consisted of groups of follicular keratotic papules mainly on the trunk and less than pinhead in size. Other lichenoid tuberculides are seen. There is a group described by Ockuly and Montgomery (1950) where the lesions occur mainly on the limbs, but other types occur with lesions elsewhere and are always associated with active tuberculosis. As their name implies, the lesions are essentially papular and they do not break down.

The remaining two conditions to be described are seldom associated with active tuberculosis, and the theory that they are tuberculides rests largely on histological evidence from the lesions themselves, which is, of course, of doubtful value. Until their true ætiology is established, dermatologists will continue to classify them as tuberculides.

Lupus miliaris disseminatus faciei presents a well-defined picture and is far from rare. Attempts have been made to differentiate it from acne agminata and acnitis, but probably all three conditions are identical. It presents as a sudden eruption consisting of papules covering the face and with a special predilection for the eyelids (Fig. 4); a few papules may also appear elsewhere on the body. Some of the lesions become pustular and break down leaving scars, whilst others fade without scarring. Groups of papules continue to appear for months or a year or two, but finally cease in their own time and do not again recur. Treatment has little effect on the course of the disease. Histologically there is a small area of necrosis surrounded by endothelial cells. In most cases the tuberculin reaction is negative or only weakly positive. Except for their skin eruption the patients usually appear fit.

Rosaceous tuberculide or micropapular tuberculide is very uncommon, but is more likely to be tubercular than the previous condition, as cases are seen from time to time in association with active tuberculosis and the response to treatment with streptomycin may be good. The condition is confined to the face and consists of minute papules dispersed amid an erythematous background. The great difficulty in diagnosis is in differentiating it from rosacea itself.

Sarcoidosis

Cutaneous sarcoidosis is relatively rare in this country, but there are many variations in its presentation. The principal forms recognised are Boeck's sarcoid, lupus pernio, erythrodermic sarcoid and the subcutaneous lesions of Darier-Roussey.

Boeck's sarcoid is probably the commonest of the cutaneous forms. The lesions are situated in the dermis and take on the form either of small nodules or larger plaques. They are firm to the touch and are either pink, yellow or blue in colour, depending to a large extent on their size and location. The mucous membranes may be involved. The lesions may occur anywhere: face, limbs, buttocks or trunk. Several examples of the nodular type have occurred following injury such as bomb blast wounds (Howell, 1946; Sweet, 1950; Rook and Davis, 1956). Histologically the lesions consist of large or smaller groups of endothelial cells, with or without giant cells, and a few lymphocytes. The giant cells may contain asteroid bodies, but asteroid bodies are not confined to sarcoidosis.

Lupus pernio is classically seen as a bulbous blue deformity on the nose, but similar lesions may occur on the ears and on the fingers and toes, classical sites for chilblains or perniosis. It is often associated with lesions of Boeck's sarcoid and the two conditions should not really be differentiated. When the fingers and toes are involved, the underlying bone often shows punched-out areas on X-ray, showing that there has been a sarcoid infiltration of the bone (Figs. 6, 7, 8).

Erythrodermic sarcoid is rare. Patches of fixed erythema with a small degree of infiltration occur on any part of the body and histologically can be shown to be due to an aggregation of miliary sarcoid nodules. Miliary sarcoid of the skin is probably not uncommon, but normally produces no symptoms and is only part of a more general condition. The subcutaneous sarcoids of Darier-Roussey are uncommon. They present as large blue deep-seated nodules on the lower legs and are easily mistaken for acrocyanosis in the early stages.

Recently there have been shown at society meetings examples of the condition known as the non-diabetic form of necobiosis lipoidica or Miecher's granuloma occurring in association with sarcoidosis elsewhere in the body, and it remains to be shown whether the association is sufficiently common to justify the condition being considered a form of sarcoidosis.

Treatment of cutaneous sarcoidosis is much less effective than of cutaneous tuberculosis. Calciferol occasionally proves successful but is usually badly tolerated, and this may well be due to the fact that in many cases of sarcoidosis the blood calcium is raised above the normal level as part of the disease. Normal antitubercular measures are not very effective and recently treatment with

ACTH and cortisone has been tried without any very great success. The dose has to be large enough to suppress inflammation and on cessation of treatment even the small improvement achieved is likely to regress. We have had insufficient experience to pass final judgement yet. The ultimate prognosis is good, but with large lesions there is certain to be some scarring when the inflammation subsides. Around the digits, clearance may be followed by considerable deformity.

Polyarteritis Nodosa

In polyarteritis nodosa skin manifestations may be due to injury to blood vessels in or near the skin or they may be of a non-specific nature secondary to disease elsewhere in the body. Only the first group are of any real importance in diagnosis. Some cutaneous changes probably occur in 25 per cent. of all cases.

The non-specific manifestations consist of urticaria, various types of erythema and œdema. Urticaria and erythema tend to occur in the early acute stage of the disease, while œdema develops later as a result of cardiac or renal damage.

The conditions due to blood-vessel involvement in or near the skin consist of purpura, gangrene, nodules, livedo reticularis and ulcerations. Purpura and subcutaneous hæmorrhages are common in the early acute stage of the disease, whilst gangrene may occur early or late but is an uncommon complication and is the result of damage to larger vessels.

Nodules are the essential feature of the disease and may occur at any stage. They tend to appear in crops, may be few or many in number and may be in the skin or subcutaneous. Their size is variable but only rarely exceeds 1 cm. in diameter. The nodules may be tender or painful and the overlying skin may be unchanged or may be red or even ulcerated. They may last for a few days only or be more or less permanent. Their great value in diagnosis lies in the fact that they can readily be excised for microscopical examination and show the characteristic histology of the disease.

Polyarteritis nodosa is normally a fatal disease of short duration, but occasionally the disease is confined to the skin for many years and, in fact, internal lesions may never occur. The characteristic lesions in this type of case are livedo reticularis and ulcerations. Livedo reticularis is an arborescent erythema not uncommon in otherwise normal persons as a transient phenomenon due to cold. In polyarteritis, however, it is permanent and is probably due to interference of the skin nutrition because of arteriolar damage. It may be localised to a limb or generalised. Ketron and Bernstein (1939) describe and give photographs of a generalised case but with associated internal lesions; more often no internal lesions are manifest. Lyell and Church (1954) list several examples of this type in their review of the cutaneous manifestations of polyarteritis nodosa. Ulcerations may appear on any part of the body but are perhaps most often seen on the lower limbs. The ulcers are indolent with much surrounding fibrosis and may show enlarged blood vessels coursing over the edge to dip down into the ulcer crater. The diagnosis in both these types of case may be established by finding the characteristic histological changes in the blood vessels in the area, but is made with greater certainty when superficial nodules are also present.

Summary

An account is given of the cutaneous manifestations of tuberculosis, sarcoidosis and polyarteritis nodosa.

Skin changes in tuberculosis may be due to the presence of tubercle bacilli living in the skin or they may be secondary to disease elsewhere in the body. In the first group the following conditions are found: primary tuberculosis of the skin, miliary tuberculosis, lupus vulgaris, tuberculosis verrucosa cutis, scrofuloderma and tuberculosis cutis orificialis. The second group consists of erythema nodosum, erythematous tuberculide, Bazin's disease, papulo-necrotic tuberculide, lichenoid tuberculides, lupus miliaris disseminatus faciei and rosaceous tuberculide.

In sarcoidosis skin lesions take on a variety of forms, the principal ones being classified in one of four main groups: Boeck's sarcoid, lupus pernio, erythematous sarcoid and the subcutaneous lesions of Darier-Roussey. Lesions in Boeck's sarcoid may be either nodular or in plaques and they are often found associated with lesions of lupus pernio.

In polyarteritis nodosa, skin changes are found in about 25 per cent. of all cases. The lesions may be non-specific and consist of urticaria and various forms of erythema or they may be due to damage to blood vessels in or near the skin. Nodules are the most characteristic of these changes, but hæmorrhages, livedo reticularis and ulcerations also occur. Occasionally polyarteritis nodosa is confined to the skin and in these cases livedo reticularis and ulcerations are the characteristic features.

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PULMONARY ACTINOMYCOSIS

RECOVERY IN A MONGOL

By D. M. Prinsley

From Middleton Hospital, Ilkley, Yorks.

Actinomycosis in man is a rare disease. The causative organism, *Actinomyces bovis* grows in colonies in the form of a branched mycelium. Macroscopically a colony has the appearance of a small granule about 1 mm. in diameter and section shows a central, partly necrotic, mass of branching filaments with a peripheral radial arrangement of clublike bodies—the "ray fungus." The organism is never found outside the body but is frequently present as a saprophyte on human tooth surfaces, dental tartar and in tonsillar crypts (Dubos, 1952). The mode of spread is unknown. Invasion of the body may occur, with the formation of a granulomatous lesion, suppuration and local extension. Invasion usually follows some break in the continuity of the mucous membrane; for example, a cervico-facial lesion may develop after a dental extraction or a fracture of mandible. The majority of cases of human actinomycosis are in the cervico-facial region, the abdomen being involved in 20 per cent., and the thorax in 15 per cent. (Cope, 1938; Topley and Wilson, 1948). Infection may reach the lungs by inhalation via the bronchi, by embolism of infected blood clot from a focus elsewhere in the body, by direct spread into the thorax from a lesion in the neck, or by perforation of the diaphragm by a lesion in the bowel or liver. There is local necrosis, tissue planes are easily crossed and bone and skin are eroded without difficulty, hence the frequency of sinus formation. Before the advent of Penicillin, the first effective form of treatment, pulmonary actinomycosis was a fatal illness. Hence the mortality figures supplied by the Registrar-General for the years before Pencillin will also indicate approximately the incidence of the disease.

Table 1.—Deaths due to Actinomycosis of Lung in England and Wales, including Cases suffering from Actinomycosis in Other Sites

Year	*Males*	*Females*
1931	8	1
1935	10	3
1938	5	2
1949	2	1

The following case is reported because it illustrates so well many of the features of pulmonary actinomycosis, both clinical and bacteriological, and also demonstrates how easily a desperately ill patient was cured by appropriate therapy.

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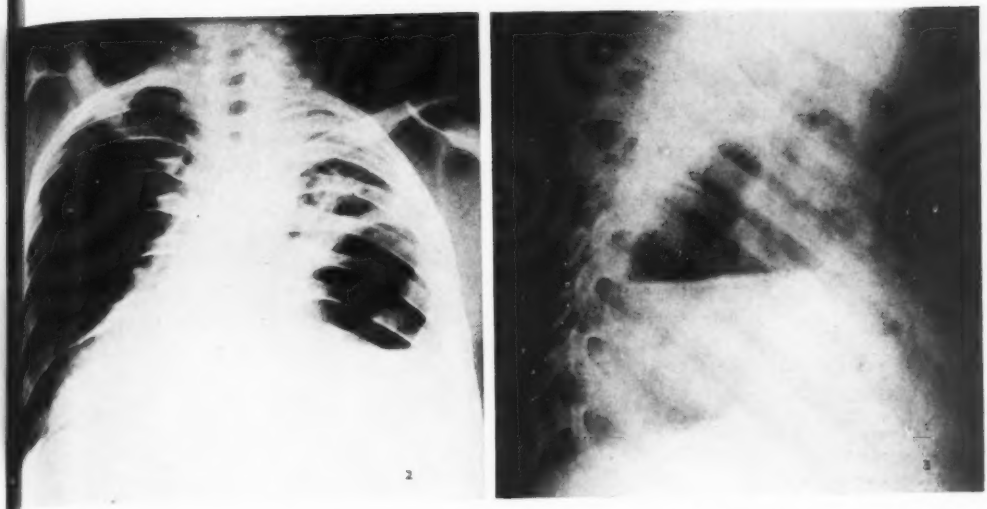

FIGS. 2 AND 3.—X-ray appearance after aspiration, showing gross mediastinal displacement, collapse of the left lung and a large quantity of air and fluid in the pleura.

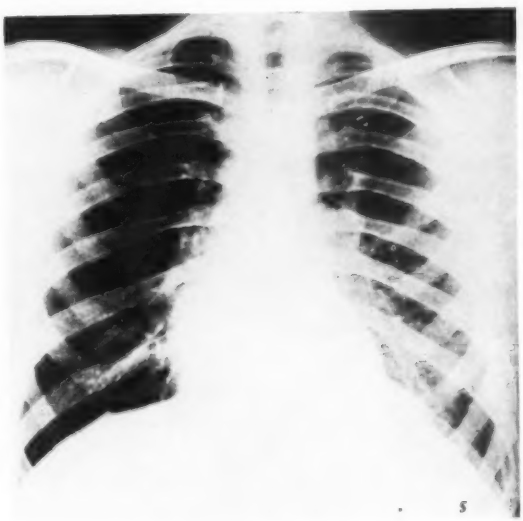

FIG. 5.—X-ray appearance after treatment. The left lung is fully expanded. There is some pleural thickening but no other abnormality.

The patient was a man aged 21 years who was an inmate of a mental defective colony. He was a well-behaved mongol who worked in the colony and was able to do simple tasks and understand orders. His mentality was equivalent to that of a boy aged 6 years. In 1949 and 1954 he had suffered from right and left lower lobe pneumonia, which on each occasion had promptly responded to sulphonamide, and allowed him to return to work within two weeks. In 1952 and 1955 he had had attacks of tonsillitis with fever. There was no other history of note.

The present illness began on 8.11.55, when the patient complained of pain over the front of the left chest, and his temperature was found to be 102° F. However, he recovered after three days and returned to work. On 22.11.55 he was again found to be febrile and râles were heard at the left base. The illness continued with varying severity. On 28.12.55 there appeared to be a left pleural effusion, and 10 oz. of straw-coloured fluid were removed by aspiration.

Report on the fluid: Abundant pus cells. No organisms seen. Culture. No bacterial growth.

Following the aspiration the patient apparently recovered and was allowed up, but on 11.2.56 he fainted and was found to have a high fever, with signs of fluid in the left pleura. A further aspiration was carried out and this time 1 oz. of purulent fluid was withdrawn.

Report on the fluid: Film shows numerous Gram-positive bacilli morphologically resembling diptheroids. No acid-fast bacilli seen. Culture: No bacterial growth aerobically or anaerobically after several days' incubation.

Over the next few days there was little change, but on 1.3.56 he started to cough up bright red blood. He was transferred to Middleton Hospital the following day. The patient had been treated with full doses of Penicillin and Sulphonamide, and also had a short course of Chloramphenicol. A summary of the illness and treatment is shown in Fig. 1.

On admission to Middleton Hospital the patient was obviously very ill indeed. He was conscious and fully orientated but unable to sit up. He had an incessant productive cough, bringing up foul-smelling reddish-brown sputum in large quantities which sprayed out of his mouth and nose over the bed and his surroundings. On examination of the chest it was evident that a large collection of fluid was present in the pleural space. The trachea was displaced to the right, and the heart was grossly displaced to the right.

An immediate aspiration was carried out and 12 oz. of foul-smelling reddish-brown fluid were removed similar in appearance to the material expectorated. A large air space with a strongly positive pressure was present above the fluid in the pleura. An empyema with broncho-pleural fistula was diagnosed, and before removing the aspiration needle, 1 mega unit of Penicillin with Streptokinase and Streptodornase was injected. The X-ray appearance after the aspiration is seen in Figs. 2 and 3. Gross mediastinal displacement is still present.

Examination of a Gram-stained film of the pus showed several clumps of Gram-positive mycelium resembling *Actinomyces bovis*. A test tube of the pus was then examined more carefully, and when a thin film was allowed to form on the glass by tilting the tube, sulphur granules could be seen, tiny whitish

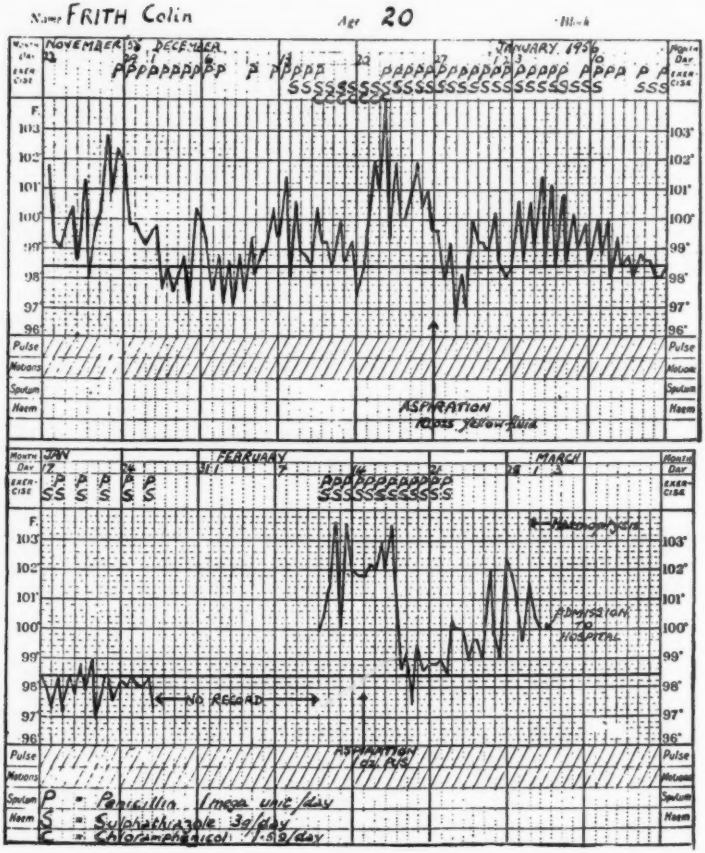

FIG. 1.—A summary of the temperature charts and treatment before admission to hospital.

specks about 1 mm. in diameter. Aerobic and anaerobic cultures of the pus were made. Six plates were cultured anaerobically with 10 per cent. CO_2, and when the plates were examined four days later typical tiny white colonies of *Actinomyces bovis* were seen on two plates. The positive plates had the same odour as the original pus. Subcultures were tested for Penicillin sensitivity, and were found to be sensitive at 0·5 unit per ml.

Other investigations of the patient showed that the hæmoglobin was 50 per cent. with 2,870,000 red cells. The WBC was 8,400 per c.mm. with 68 per cent. neutrophils, 30 per cent. lymphocytes and 2 per cent. monocytes. The blood sedimentation rate was 144 mm. in one hour. The serum albumen was 2 G. per cent., and the serum globulin 4·5 G. per cent. Total—6·5 G. per cent. The Mantoux reaction was negative.

Treatment was started the day after admission with Penicillin 2 mega units morning and evening, by injection, and with Sulphatriad 1 G. four-hourly by

mouth. (At the time the previous prolonged treatment with sulphonamide was not known.)

Further aspirations were carried out on 5.3.56 and on 16.3.56 and on each occasion Penicillin with Streptokinase and Streptodornase was injected into the empyema space. Typical *Actinomyces bovis* filaments were seen in the pus. Potassium iodide was given in full doses, but this provoked an iodide eruption after two weeks and was then abandoned. The patient also received iron and vitamins by mouth.

Recovery was slow and uninterrupted. A crop of boils, apparently the remnants of the iodide eruption, responded promptly to a short course of aureomycin. The patient's general condition improved and his appetite returned within a few days of starting treatment. The productive cough ceased after the second aspiration and thereafter the only respiratory symptom was a slight cough without sputum. A summary of the temperature charts is seen in Fig. 4. Note the rapid gain in weight.

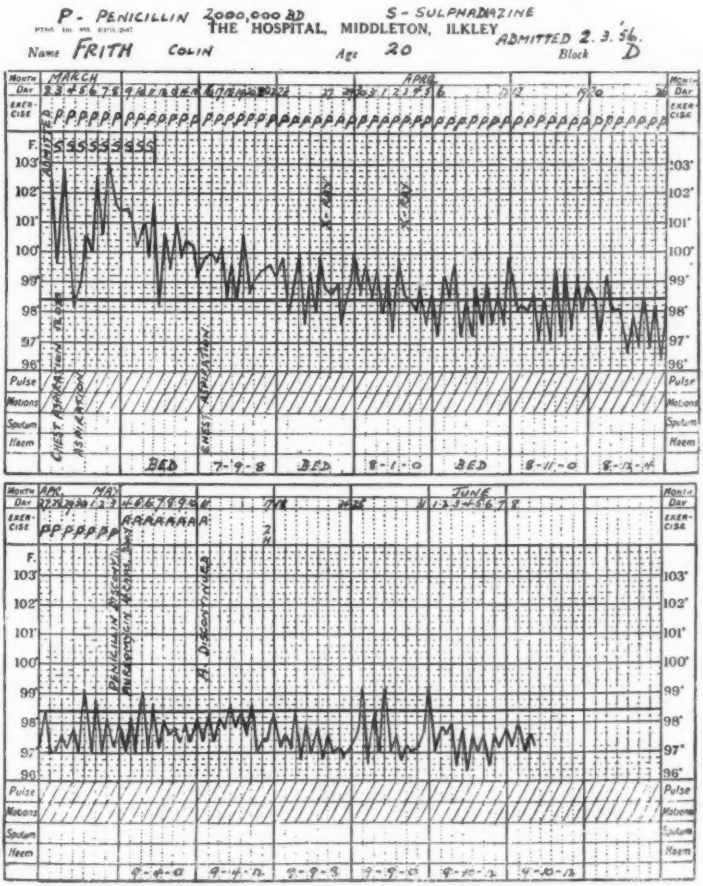

FIG. 4.—A summary of the temperature charts and treatment in hospital.

Treatment was stopped after ten weeks. The lung was fully expanded and the diaphragm moved normally on screening. Slight pleural thickening appeared to be the only abnormality. A left bronchogram showed a normal bronchial tree and tomography of the left lung was normal. The teeth were examined by the dental surgeon (Mr. S. Levinson) and were found to be perfect, without caries and without tartar. The tonsils were examined by the E.N.T. surgeon (Mr. J. H. Otty), who found chronically enlarged tonsils but no clinical evidence of actinomycotic infection. The tonsils were swabbed and anærobic cultures of the tonsillar debris revealed typical *Actinomyces bovis* colonies. Subcultures were sensitive to various antibiotics (Table 2).

TABLE 2

Penicillin ..	..	2·5 units per ml.
Aureomycin ..	..	10 microgramme per ml.
Erythromycin	..	10 " " "
Terramycin ..	..	10 " " "
Tetracycline	..	10 " " "
Chloramphenicol	..	40 " " "
Streptomycin	..	80 " " "

The hæmoglobin rose to 105 per cent. with 5,200,000 red cells per cu. mm., the W.B.C. was 6,400 cu. mm. and the E.S.R. was 8 mm. in one hour.

The tonsils were removed by dissection under general anæsthesia on 4.6.56 and subsequently were cut into fragments, but attempts to grow *Actinomyces* were unsuccessful.

The final X-ray appearance is seen in Fig. 5. The patient was then discharged.

Discussion

The diagnosis of actinomycosis depends upon recovery of pus from the lesion. Very little help can be gained by other investigations. In this case the disease process followed its usually described course with localisation in one lower lobe, followed by early pleurisy with effusion of straw-coloured fluid which subsequently became purulent. The laboratory report on the purulent fluid aspirated on 14.2.56 mentioned numerous Gram-positive bacilli morphologically resembling diphtheroids. These were undoubtedly fragments of actinomycotic mycelium. If a sulphur granule is finely ground up the stained film closely resembles the "Chinese letters" appearance of diphtheroid bacilli, but careful examination will reveal true branching and the colony character and rate of growth are quite different.

The tendency for an actinomycotic empyema is to extend through the chest wall and discharge through one or more sinuses. Indeed it is usually at this stage that the diagnosis is made. However, this patient ruptured his empyema into a bronchus and partly relieved the considerable pressure by coughing up some of the contents. No doubt the hæmoptysis immediately before admission to hospital coincided with the formation of the broncho-pleural fistula. The sputum appeared to be the same as the empyema contents removed by aspiration. Actinomyces were not seen in the sputum, although they were readily seen in the aspirated pus. Garrod (1952) points out that it is unusual to find *Actinomyces* in sputum and doubts if sputum findings should ever be the basis for diagnosis.

The well-known sulphur granules in actinomycotic pus are not really obvious unless looked for carefully. If the pus is diluted about five times with water the granules will settle to the bottom and become readily apparent. The cultural characteristics of the organism showed that it was a strict anaerobe growing in 10 per cent. CO_2 on blood agar plates. The order of sensitivity to antibiotics (Table 2) was similar to that demonstrated by Garrod (1952), who found the greatest sensitivity to Penicillin and the least to Streptomycin.

X-ray investigation is not helpful. Long-standing cases may be impossible to differentiate from tuberculosis. Even a miliary or bronchopneumonic picture may be seen. But the typical features described by Schinz *et al.* (1953) are that the disease is unilateral in a lower lobe, there is early and extensive pleural involvement and there is lack of bronchogenic spread. One peculiar feature may be an ossifying periostitis of the chest wall. No hint of the diagnosis was evident in this patient although the radiograph fulfilled most of the above conditions.

The most impressive feature of the illness was the response to treatment during the first four weeks. Although before admission the patient had received large doses of Penicillin and Sulphonamide, even larger amounts of Penicillin were clearly necessary. Nichols and Herrel (1948) reported four failures out of nine cases of pulmonary actinomycosis treated with up to 1 mega unit of Penicillin daily.

Culture of *Actinomyces bovis* from this patient's tonsils showed the source of his pulmonary infection. Mongols suffer from a defective, atrophic nasal and bronchial mucosa which makes them very susceptible to respiratory infections. Engler (1949) reported pulmonary disease, chiefly tuberculosis and broncho-pneumonia, as the cause of death in 92 per cent. of his cases, and quoted other series with an 80-90 per cent. mortality from respiratory disease. Therefore, there was a clear indication to remove the tonsils which still harboured *Actinomyces bovis* after prolonged chemotherapy. I have been unable to find any reference in the literature to actinomycosis as a cause of illness or death in mongols.

Summary

A description is given of an adult mongol who developed pulmonary actinomycosis with an empyema and broncho-pleural fistula. Some of the features of bacteriological diagnosis are demonstrated. The illness was cured by aspiration and heavy and prolonged dosage with Penicillin.

It is a pleasure to thank Mr. R. A. Smith, A.I.M.L.T., Senior Technician, for help with this case. He identified the clumps of actinomyces in the first specimen of pus examined and successfully cultured the organism and carried out the sensitivity tests. I am also grateful to Dr. A. H. Stewart for his most informative notes about the patient prior to his hospital admission.

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ATYPICAL PNEUMONIA

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The syndrome "Atypical Pneumonia" comprises that group of pneumonias which shows little or no response to the known antibiotics, has distinct clinical, radiological and laboratory features, and is produced by different ætiological agents, many of which are as yet unknown.

A study of "Atypical Pneumonia" as seen in hospital, industrial and private practice was begun in the spring of 1952. The fact that a serological diagnosis in atypical pneumonia can only be made retrospectively and that an ætiological agent can only be isolated in less than 20 per cent. of such cases suggested the necessity for seeking clinical, hæmatological and radiological characteristics to assist in the diagnosis and treatment of these pneumonias. By this means two distinct types of atypical pneumonias—aspiration and viral—have been distinguished. The correlation of the clinical features to the X-ray findings and the particular differential white blood cell counts and the serological changes in each variety have been demonstrated. In addition attention has been drawn to the relationship and differentiation of aspiration pneumonia and pulmonary atelectasis.

For the purpose of this research all cases of pneumonia were analysed. These included cases which subsequently proved to be segmental atelectasis, infarct, carcinoma and tuberculosis. From this study 135 cases conforming to "Atypical Pneumonia" were included in the series; they comprised 45 cases from the Royal Chest Hospital, 23 cases from industry, 41 cases from the Hampstead General Hospital, and 26 from private practice.

The method of investigation adopted was:

1 Age and sex.
2 Past history of respiratory diseases.
3 Family history.
4 Mode of onset—insidious or abrupt.
5 Possible contacts—human, avian or animal.
6 Presenting symptoms.
7 Physical signs—upper and lower respiratory tract.
8 Sputum examination for organisms.
9 Blood sedimentation rate.
10 Differential white blood cell counts, blood cultures.
11 Serological tests for cold agglutinins and immune bodies.
12 Serial X-rays of the chest.
13 Course and duration.
14 Complications.
15 Treatment and Results.
16 Conclusions.

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Age and Sex

The ages ranged from 6 to 78 years, being made up of 80 males and 55 females. Of the 90 cases of aspiration pneumonia in this series 46 were males and 44 females. Of the 45 cases of virus pneumonia, 34 were males and 11 females. The number of cases occurring in the various age groups among the males and females is shown in Table 1.

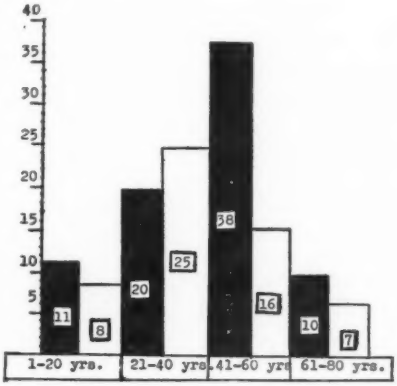


Table I.—Age and sex. Solid = Males; Open = Females.

Past History

There was a past history of respiratory disorder in 59 cases: 21 with recurrent bronchitis, 15 with pneumonia, 10 with pleurisy, 4 with asthma, 3 with chronic naso-pharyngeal catarrh, 3 with influenzal bronchitis, and 3 with pulmonary tuberculosis. There appears to be no relationship between the past history and this syndrome.

Family History

Only 10 cases gave a family history of respiratory disease: pulmonary tuberculosis in 4, asthma in 2, carcinoma lung in 1, and bronchitis in 3 cases. Again no clinical relationship to this disease was noted.

Mode of Onset

The mode of onset was insidious in 90 cases and abrupt in 45. Of these 60 presented as upper respiratory infections, 50 as presumably virus infections, 20 as bronchitis or lower respiratory disease, and 5 cases as cardiac disorders. Most cases with an insidious mode of onset presented with upper respiratory signs and symptoms and a few with signs and symptoms of bronchitis. The cases with an abrupt mode of onset presented as influenzal or other virus-like infections with predominance of constitutional signs and symptoms before inflammatory lung signs appeared.

The prodromata before evidence of lung involvement was one to five days in 45 cases, five to ten days in 65 cases, and ten to fifteen days in 25 cases.

Retrospectively 90 cases of the aspiration type—60 with upper respiratory presenting signs and symptoms, 25 with bronchitis signs and symptoms, and 5 with cardiac signs and symptoms at the onset and 45 cases of the virus type with constitutional symptoms predominant were separated.

Possible Contacts

Possible contact with human, avian or animal infective agents was not undertaken in this series because of the limited facilities available at the time.

Presenting Symptoms

In order of frequency these were: *Cough*—108 cases (63 non-productive and 45 productive), 77·5 per cent. *Chest Pain*—78 cases, 56 per cent. *Constitutional* (rigors, malaise, lassitude)—69 cases, 50 per cent. *Fever*—54 cases, 40 per cent. *Upper Respiratory* (sore throat, coryza, sinusitis)—60 cases, 44·5 per cent. *Dyspnœa*—38 cases, 30 per cent. *Hæmoptysis* (rusty sputum)—19 cases, 15 per cent. *Miscellaneous* (vomiting, anorexia, epigastric pain, frontal headache) 14 cases, 11 per cent.

Constitutional symptoms, dyspnœa and cough appearing early and continuing throughout the course of the illness were a feature of the virus type of pneumonia; whereas upper respiratory symptoms with localised pain, fever and cough appeared in the early stages of the aspiration type of pneumonia. The clinical significance of the presenting symptoms in distinguishing the two types of atypical pneumonia becomes of major importance.

Physical Signs

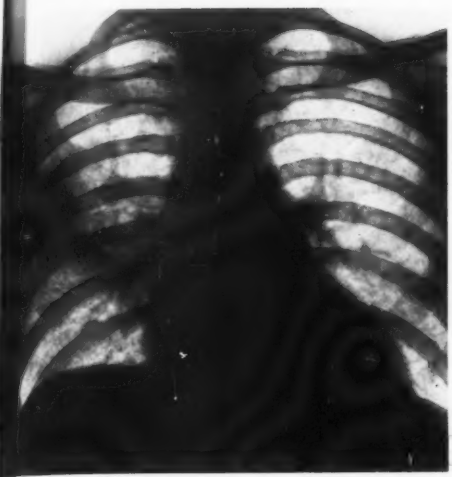
Although investigations made by others stress the paucity of physical signs, such signs were definitely detected during the course of the illness in this series. Upper respiratory signs, localised chest pain and signs of atelectasis followed by consolidation were noted in two-thirds of the cases of aspiration pneumonia. On the other hand, definite physical chest signs in cases of virus pneumonia were not detected. An analysis of the physical signs noted in the series were: *Râles* (fine and coarse) with slight impairment of the percussion note in 75 cases (54 per cent.); *diminished air entry* in 64 cases (47 per cent.); *bronchial breath sounds* in 52 cases (40 per cent.); *inspiratory rhonchi* in 28 cases (21 per cent.); *pleural friction sounds* in 14 cases (10·5 per cent.); and *upper respiratory signs* (rhinitis, pharyngitis and sinusitis) in 46 cases (33 per cent.)

Sputum Examination

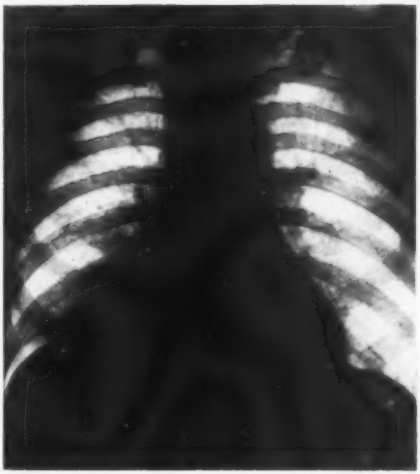
Sputum and post-nasal swab examinations were undertaken in 100 cases. In 4 cases tubercle bacilli were found. In 40 cases pneumococci were isolated and in 5 cases staphylococci, while in 3 cases monilia were present. In no less than 48 cases mixed non-pathogenic bacteria were found.

Blood Sedimentation Rate

The blood sedimentation rate (Westergren) was determined in 110 cases. Table 2 shows the number of cases, sputum findings, type of pneumonia and anatomical variety according to the blood sedimentation rates.



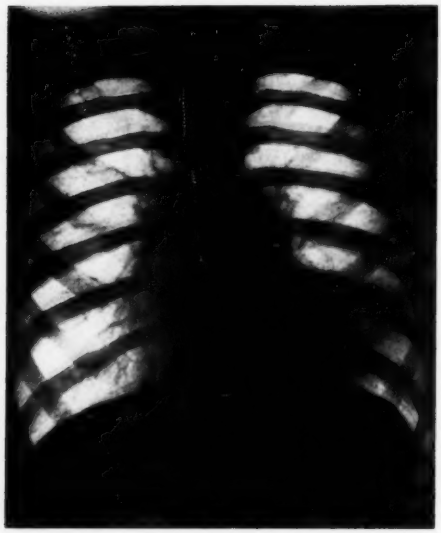
E 1.—Consolidation with atelectasis. Lateral middle segment of right middle lobe.



CASE 2.—Consolidation of right anterior basic segment and cardiac segment.

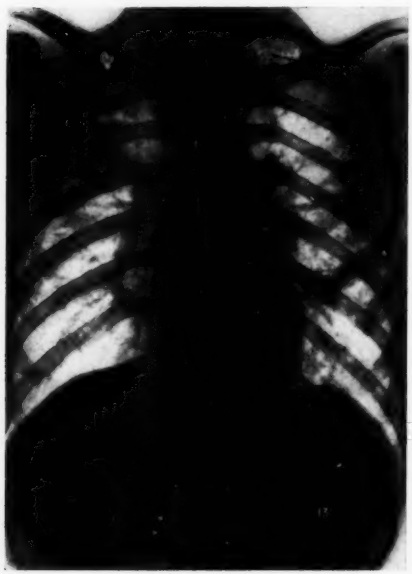
CASE 4.—Consolidation left lower lobe and lingula.

CASE 6.—Consolidation and atelectasis of apico-posterior and antero-lateral segments of left upper lobe.

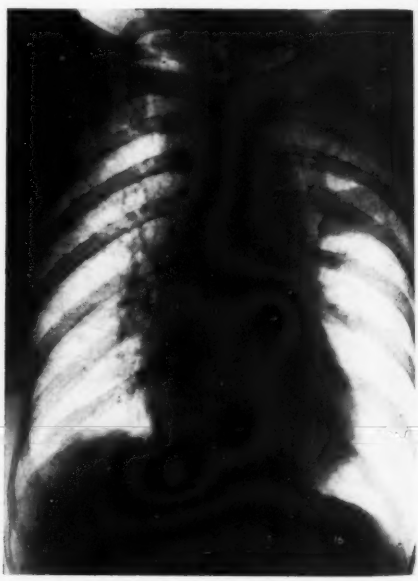


CASE 9.—Consolidation lateral middle segment of lingula.

CASE 11.—Consolidation of anterior and later middle segments of right middle lobe wi atelectsis.



CASE 13.—Consolidation adjacent to hilum (dorsal segment) and postero-lateral segment of right upper lobe.



CASE 16.—Consolidation antero-lateral segment of left upper lobe with pulmonary cyst.

TABLE 2

B.S.R.	*Cases*	*Organisms*	*Type*	*Variety*
3–10 mm.	17	12 non-paths.	virus. atelect.	lobular
11–22 mm.	42	36 non-paths.	aspirat. pneum.	segmental
23–60 mm.	51	35 pathogens, pneumo., staph., streps., Friedlander bacilli	aspirat. pneum.	lobar

It can be said that blood sedimentation rate estimation affords a useful diagnostic criterion in distinguishing segmental atelectasis, viral and aspiration pneumonias due to non-pathogens and pathogens.

DIFFERENTIAL WHITE BLOOD CELL COUNTS

The differential white blood cell counts were undertaken in 78 cases. The number of cases, sedimentation rates, pathogenic, non-pathogenic or viral types are grouped in Table 3.

TABLE 3

W.B.C.	*Cases*	*B.S.R.*	*Type*
4,000–8,000	17	4–10 mm.	viral
8,000–12,000	34	11–20 mm.	non-pathogen
13,000–30,000	26	20–60 mm.	pathogen

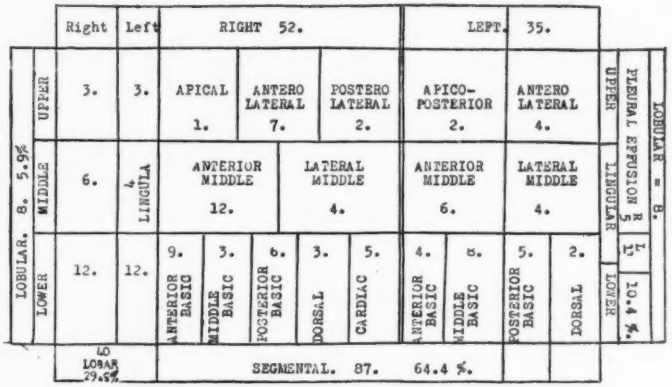
In pure pathogenic bacterial infections, the neutrophil increase was marked, in mixed bacterial infections they were moderately increased, whereas in the non-pathogenic and viral infections they were hardly increased; in fact, in the viral types, neutropenia was a feature with lymphocytosis in the early phase of the disease. Although in both the viral and aspiration types the eosinophiles increased in number during convalescent period, this increase was markedly greater and persistent throughout the illness in the viral type. It can be concluded that the total and differential white blood cell counts and the eosinophil estimations were of clinical diagnostic and prognostic value in cases of atypical pneumonia. In only 3 cases positive cold agglutinins (1 in 20 titres) at the end of the second week of the illness were present. Other workers have found that the presence of cold agglutinins have neither diagnostic nor prognostic significance.

SERIAL X-RAYS OF CHEST

Radiologically, the anatomical diagnosis in the series was determined by noting the areas of consolidation and atelectasis in relation to the bronchopulmonary segments of the lung. These pneumonias did not give the denseness characteristic of the classical lobar or lobular pneumonias of bacterial infection, although they did show lobar, segmental, sub-segmental or lobular distribution.

The aspiration pneumonias tend to be more clear-cut in the anatomical outlines than the viral pneumonias. The bacterial pneumonias commonly present as lobar consolidation when pneumococci, staphylococci, streptococci and/or Friedlander bacilli are present. The non-pathogenic pneumonias, on the other hand, occur as segmental or sub-segmental consolidation, while the viral pneumonias tend to overlap segments or sub-segments to involve more than one lobe and are often bilateral. In the series consolidation of the right lung was noted in 65 cases, of the left lung in 52 cases, and of both lungs in 8 cases. Table 4 illustrates the number of cases of atypical pneumonia according to their lobar, segmental and lobular distribution.

TABLE 4



COURSE AND DURATION

The cases were divided into five groups. Table 5 illustrates the number of aspiration (lobar and segmental) and viral pneumonias which occurred in each group. Six cases in this series were not followed up.

TABLE 5

Cases	*Group*	*Type*	*Lobar*	*Segmental*	*Virus*
63	I	Short and mild	10	35	18
41	II	Short and severe	20	5	16
16	III	Prolonged and mild	3	3	10
9	IV	Prolonged and severe ..	3	6	0
6	V	No records	4	1	1
			40	50	45

COMPLICATIONS

In the series 73 cases developed complications during the course of the illness. They are tabulated in Table 6.

TABLE 6

Cases	*Complications*	*Lobar*	*Segmental*	*Virus*	*Lobular*
17	Pleural effusion	6	9	2	—
6	Partial fibrosis	4	2	—	—
12	Congest. ht. fail.	6	2	3	1
8	Bronchitis	4	1	—	3
3	Emphysema	2	—	—	1
10	Asthma	3	3	2	2
5	Bronchiectasis	4	1	—	—
2	Empyema	2	—	—	—
2	Bronchial N.G.	2	—	—	—
3	Tuberculosis	—	3	—	—
9	Sinusitis	2	7	—	—
1	Encephalitis	—	—	1	—
3	Uræmia	—	—	2	1
2	Rheu. arthritis	—	—	2	—
4	Anæmia	2	—	2	—
87		37	28	14	8

TREATMENT AND RESULTS

In this series 129 cases were treated symptomatically and/or with sulphonamides, penicillin, aureomycin, streptomycin, oxygen, carbon dioxide, pumulotherapy, convalescent serum and gamma globulin. The number of cases treated with one form of therapy and the results are documented in Table 7. Twenty-six cases were given two forms of treatment and 6 cases three forms of treatment at the same time.

TABLE 7

Treatment Cases	*Results*		*Complications*					
	Rec.	*Died*	*CB/E.*	*T.B.*	*N.G.*	*Bronchiectasis.*	*Fibrosis*	*Asthma*
Symptomatic (50)	48	2	3	2	—	—	1	2
Sulphonamide (28	22	6	2	—	1	1	—	—
Aureomycin (9)	8	1	—	—	1	—	1	—
Penicillin (45)	38	7	—	2	2	2	5	4
Streptomycin (4)	4	—	—	2	—	—	1	—
O, CO and pumulotherapy (9)	6	3	—	1	—	1	1	—
Convalescent serum (2) ..	2	—	—	—	—	—	—	—
Gamma globulin	1	—	—	—	—	—	—	—

CONCLUSIONS

Full investigation to include bacteriology and serology is a major undertaking in a large series, and so far none has been published to assist in the diagnosis and treatment of these pneumonias. In this series it has been noted that the mode of onset, the presenting symptoms, physical signs, X-ray features, blood counts and blood sedimentation rates afford the best diagnostic criteria.

Aspiration Pneumonia (*Atypical*) is a descriptive term. Its pathogeny may be attributed to blockage of the second or third degree bronchus with inspissated mucus plug and the result of diminished ciliary action and the cough reflex, and the accumulation of secretion in the respiratory tract. It occurs frequently in association with acute infections of the upper respiratory tract (the inflammatory consolidation which is localised to a lobe or segment is associated with a degree of atelectasis) and occasionally in association with chronic bronchitis or bronchiectasis (the inflammatory consolidated zones are scattered, diffuse and involve several lobes or segments). The mode of onset is invariably insidious. The respiratory symptoms are predominant, whereas the constitutional symptoms are mild and variable. Cough, which is present early, is hacking, troublesome and persistent. Expectoration appears later in the course of the disease and is scanty, sticky and mucoid, being sometimes streaked with blood. Pain and tenderness are localised to the site of the lesion. The physical signs are not conclusive of definite consolidation but of a lobar or segmental inflammatory zone. There is slight impairment of the percussion note, harsh breath sounds are present and minimal inspiratory crepitations. The *blood sedimentation rate* is usually raised above 20 mm. when pathogenic bacteria are present and below 20 mm. when non-pathogens are present. The differential white blood cell counts show a marked neutrophil increase with a total count of over 12,000 in pathogenic bacterial infections but a total count of 6,000 to 9,000 with moderate neutrophil increase in non-pathogenic infections. *Chest X-ray findings* afford an early diagnosis in conjunction with the minimal physical signs and symptoms. The woolly area of increased density which bears relation to the site of the pain varies in size from a shilling to that involving the whole lobe. This area is less dense but more mottled than that of classical pneumonic consolidation. Its outlines are definite, and since its spread appears to begin at the hilum it has a triangular appearance.

When the right middle lobe or the lingula of the left upper lobe or their segments are involved the triangular shadow tends to be flattened and lies towards the right or left border of the heart. On lateral X-ray the triangular opacity lies anteriorly. Compensatory emphysema of the anterior basic segments of the lower lobes permit visualisation of the posterior border of the heart, while the septum between the triangular area and its adjacent lobe is also clearly seen.

When the lower lobes and their segments are affected the triangular shadow occupies a posterior and medial position towards the spine. The hilar shadow is depressed and the adjacent lobes show compensatory emphysema. The lateral X-ray demonstrates it, for here the anterior edge of the triangular shadow is seen to lie against the depressed and curved greater fissure, while the whole triangular shadow, with its broncho-vascular striations crowded together, occupies the posterior half of the raised diaphgram.

When the upper lobes and their segments are affected, the triangular shadow lies anteriorly and medially towards the anterior chest wall and obliterates the space between the sternum and ascending aorta. The hilar shadow moves upwards and is indistinct at its upper margin. There is compensatory emphysema of the lower and middle lobes. The trachea is deviated towards the triangular shadow together with the superior mediastinum, while the broncho-vascular striations are not so well defined as those in the lower lobe affection.

	Case 1	Case 2	Case 3	Case 4
Age	45 years	18 years	15 years	46 years
Sex	Male	Male	Male	Male
Occupation	Woodworker	Army national service	School boy	Builder's labourer
Onset	Insidious, following influenza	Insidious, with URT infection	Abrupt with ac. resp. inf.	Insidious, antecedent, des. URT infection
Present symptoms	Pyrexia, cough, scanty sputum, pain rt. axilla, malaise	Cough, pain rt. chest, sore throat; rigors, slight fever	Cough, fever, malaise, rusty sputum, pain rt. chest	Pain lt. chest, rigors, fever, cough, scanty sputum, coryza
Physical signs	IPN, DAE, Ins. creps. RMZ and BBS	DM, IPN, râles RLZ, inflamed fauces	DPN, BBS, IVR, fluid rt. base	DPN, BBS, IVR, ins. creps. LLL
Blood sed. rate	50 mm., 8/52 wks. 6 mm.	20 mm.	—	40 mm.
Sputum	*Staph. aureus*	Non-pathogens	Non-pathogens	Mixed growth, pneum.
W.B.C. counts	10,000 polys. 82%	10,000 polys. 75%	4,500	11,00 polys. 71%
X-ray	Consolidation lat. mid. segment RML with antelectasis	Rt. ant. basic seg. and cardiac segment	Con. RML, RLL with pleural effusion	Consolidation LLL and lingula
Course	Prolonged and severe, 10 weeks	Short and mild, 3 weeks	Prolonged and severe, 10 weeks	Short and mild, 3 weeks
Complications	Nil	Nil	Partial fibrosis	Nil
Treatment	Symptomatic, breathingexer., O and CO_2	Sulpha and penicillin	Penicillin, aureomycin and streptomycin	Sulphadiazine
Results	Com. recovery	Com. recovery	Slow resolution	Complete
Type	Aspiration	Aspiration	Virus	Aspiration

	Case 5	Case 6	Case 7	Case 8
Age	60 years	62 years	33 years	48 years
Sex	Male	Male	Male	Male
Occupation	Civil servant	Bank manager	Labourer	Labourer
Onset	Acute, influenza-like	Insidious with coryza and URT infection	Abrupt. URT infection	Abrupt, influenza-like
Present symptoms	Cough, fever, pain lt. lower chest rigors	Pain lft. upp. chest, cough, streaky hæm., sinusitis	Sore chest, cough, scanty sput., rhinitis, pyrexia and malaise	Pain lt. chest, cough, pyrexia, rigors and dyspnœa, streaky stained sputum
Physical signs	DPN, BBS, signs of pleural effusion	IPN, BBS, rhonchi and râles LUL	DM, IPN, DAE, ins. creps. RMZ	DPN, BBS, ins. creps. lt. middle and lower zones posteriorly
Blood sed. rate	—	5 mm.	40 mm., 6/52 wks., 15 mm.	50 mm.
Sputum	—	Non-pathogens	Mixed growth with non-pathogens	Staphyloccoci and pneumococci
W.B.C. counts	12,000 polys. 85%		11,500 polys. 84%	
X-ray	Lt. mid. basic seg. with pleural effusion	Atelectasis and con. apico-post. and ant. lat. seg. LUL	Con. and collapse anterior middle segment RML	Cons. lingula and LLL with effusion
Course	Prolonged and mild, 8 weeks	Short and severe, 2 weeks	Prolonged and severe, 8 weeks	Short and mild, 3 weeks
Complications	Pleural effusion	P.T. cavity RUL	Partial fibrosis	Pleurisy
Treatment	Penicillin and aspiration	Quinine, CO_2 and O, A.P. with oil and strep.	Penicillin and symptomatic drugs	Aureomycin and sulphonamides
	Slow			Complete
Type	Virus	Aspiration	Aspiration	Virus

TABULATED CASE REPORTS (*Continued*)

	Case 9	*Case* 10	*Case* 11	*Case* 12
Age	59 years	49 years	30 years	58 years
Sex	Male	Male	Male	Male
Occupation	Manager		Building trade	Cleaner
Onset	Insidious, URT, infection	Acute upper res. infection	Abrupt and influenza-like	Insidious with bronchitis
Present symptoms	Laryngitis, ache lt. chest, cough, nasal catarrh	Cough, dyspnœa, wheeze, fever	Fever, sore throat, cough, pain in RMZ and dyspnœa	Pain in rt. chest nr. sternum, dry cough, fever
Physical signs	IPN, DAE, in LMZ, generalised rhonchi and kyphoscoliosis	Gen. bronchospasm and signs of lt. basal consolidation	Rhonchi and poor air entry RMZ	IPN, BBS, râles and rhonchi ant. RMZ with emphysema
Blood sed. rate	20 mm. 4/52 wks. 10 mm.	7 mm.	25 mm., 3/52 wks. 5 mm.	20 mm., 10/52 wks. 10 mm.
Sputum		Mixed growth with non-pathogens	Mixed growth with non-pathogens	Rusty
W.B.C. counts	8,000 polys. 68%	3,000 polys. 85%		
X-ray	Shadow lateral middle seg. ling.	Con. RML more than lingula and LLL	Triangular opacity anterior and lateral	Resolving con. RML and cardiac segment
Course	Prolonged and severe, 14 weeks	Short and mild, 4 weeks	Short and mild, 10 days	Short and severe, 10 weeks
Complications	Hypertension	Asthma	Bronchospasm and asthma	Bronchiectasis
Treatment	Symptomatic drugs, CO_2 inhalation	Penicillin, aureomycin, sulphonamides	Symptomatic drugs	Penicillin
Results	Delayed	Complete resolution with asthma	Complete with asthma	Bronchiectasis
Type	Aspiration	Aspiration	Virus	Aspiration

	Case 13	*Case* 14	*Case* 15	*Case* 16
Age	34 years	28 years	41 years	59 years
Sex	Male	Male	Male	Female
Occupation	Electrician	Clerk	Cleaner	Factory hand
Onset	Abrupt with bronchospasm	Insidious following influenza	Insidious with URT infection	Insidious following influenza
Present symptoms	Wheezy chest, dyspnœa and fever	Cough and malaise	Persistent cough with coryza	Pain in LUZ and side, antritis, malaise, fever, cough, sputum
Physical signs	Bronchospasm with DAE interscapular region	Nil definite	Creps. left apex anteriorly, trachea to left.	IPN, BBS, rales LUZ
Blood sed. rate	30 mm.	8 mm.	36 mm., 4/52 wks. 10 mm.	25 mm., 2/52 wks. 6mm.
Sputum		Rusty		Non-pathogens
W.B.C. counts	15,000, eosin 2,600	9,000 polys. 70%		12,000 polys. 80%
X-ray	Patchy con. adj. to hilum and pos. lat. seg. RUL dorsal seg.	Pneumonitis ant. lat. segment RUL	Con. LUL with cavitation apico-posterior segment	Con. antero-lateral seg. of left upper lobe with pul. cyst.
Course	Short and mild, 2 weeks	Short and mild, 3 weeks	Short and severe, 4 weeks	Prolonged and mild, 8 weeks
Complications	Asthma and pleurisy	Nil	Unresolved fibrosis	Pulmonary cyst
Treatment	Adrenalin, ephedrine, carboserin and NAB	Symptomatic drugs	Penicillin	Penicillin, terramycin and symptomatic drugs
Results	Complete but delayed	Complete	Delayed with fibrosis	Complete with cyst outline
Type	Aspiration	Virus	Aspiration	Aspiration

The course of these pneumonias can be either mild or severe, their duration is rarely prolonged. Recovery is invariably complete. Complications, if they do arise, are confined to the respiratory system, such as permanent collapse leading to partial fibrosis, abscess, bronchiectasis and pleural effusion or adherent pleura. Patients should be kept in bed for at least one to two weeks after the temperature has returned to normal. Symptomatic treatment consists of expectorants and linctuses for the cough and expectoration, poultices and anodynes for the chest pain, and antipyretic drugs for the headache and pyrexia. Specific treatment, such as antibiotics, has a favourable response in the pathogenic bacterial infections. In non-pathogenic bacterial infections there is a good response to inhalations of oxygen and carbon dioxide, quinine and pumulotherapy. A period of convalescence should be insisted on with regular breathing exercises for at least six weeks.

Virus Pneumonia (*Atypical*). It is known that viral agents assume dual rôles *in vitro*, namely neurotrophic and hæmatotrophic. For the production of atypical pneumonia these viral agents must therefore assume the hæmatotrophic rôle. The radiological features of scattered diffuse small areas of consolidation with hilar congestion in this type of pneumonia suggest that the virus gains entrance via the lymphatics and later appears in the systemic and pulmonary blood circulation. Clinical observation supports the view that virus pneumonia tends to occur in epidemic form, although sporadic cases are known to occur on occasions. The onset is mostly abrupt. The constitutional symptoms—fever, malaise, muscular pains, rigors, vomiting—appear early, are predominant and severe, but the respiratory symptoms appear later and are mild and transient. Cough, chest pain and localised tenderness are not characteristic features. The physical signs are bizarre and not conclusive. Radiologically the features are totally unlike that of aspiration pneumonia. There is overlapping of the segmental shadows; these are more diffuse and not clearly defined; hilar congestion is always seen but there is no predilection for the basal zones. Serological diagnosis and isolation of the viral agent are possible only later in the course of the disease. With good technique and laboratory facilities the nasal and throat washed secretions can demonstrate the virus present in many cases. The blood sedimentation rate may be normal or slightly raised but seldom above 14 mm. per hour. The total white blood cell count may be below normal with neutropenia and a relative lymphocytosis. Eosinophiles appear early in the illness and increase rapidly throughout the convalescent stage to persist for several weeks. There is a high titre agglutination reaction by the end of the second week of the infection. Sometimes the Wassermann reaction is positive. The course of the illness may be mild or severe and its duration prolonged. Recovery is delayed while convalescence is often protracted. Complications are not confined to the respiratory system, indeed encephalitis, encephalo-myelitis, meningitis, jaundice and other toxic complications are often encountered in this type of pneumonia. Recent reports and the findings suggest that the newer antibiotics do not have a favourable response in a number of these cases, whereas convalescent serum and gamma-globulin certainly prevent the constitutional complications and lessen the gravity of this illness.

Summary

A study of 135 cases as conforming to the syndrome " Atypical Pneumonia " which occurred in hospital, industrial and private practice was undertaken to determine the clinical, radiological and hæmatological characteristics essential in diagnosis, prognosis and treatment of this disease.

Detailed analysis of the sex and age incidence, past history, mode of onset prodromata, presenting symptoms, physical signs, X-ray features, differential white blood cell counts, blood sedimentation rates, course, complications, treatment and results have been documented and their significance noted.

A classification and description of the types and varieties of atypical pneumonia is given.

Case history of 16 cases has been appended together with X-ray photographs to illustrate the types and anatomical sites of atypical pneumonias.

This work was supported by a grant from the Endowment Fund of the Royal Free Hospital Group, made to the late Dr. F. E. Saxby Willis of the Hampstead General Hospital.

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DEVELOPMENT ANOMALIES OF THE RESPIRATORY TISSUE

By S. Engel

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Developmental anomalies of the pulmonary parenchyma tend to be overlooked because they are less conspicuous than gross malformations as, for instance, agenesis of lobes or parts of lobes. It is the purpose of this paper to draw attention to congenital anomalies of the respiratory tissue and the possible connection of such anomalies with pathological changes. The many factors involved in cystic disease have been indicated by Ellman (1952) and the lack of knowledge on this subject is pointed out by Coope (1948) who, dealing with cystic lung, comments: "It is strange that very few examples of the condition have been described in the fœtus; more certain knowledge should be available in the future, now that the developmental anomalies of the lung are likely to be looked for with more lively interest than in the past."

I should like to record the clinical and anatomical details of four cases, as this may be helpful to others who have an opportunity of following up this line of investigation.

Case 1. A baby, born at term, was of normal shape and weight. It developed breathing difficulties soon after birth and died within a few hours. Post-mortem examination showed the lungs semi-collapsed and histologically they were mainly fœtal in character. Death was due to respiratory failure.

Comment. The intra-uterine differentiation of large parts of the lung had been arrested at an early stage. Some areas were normally developed. Other organs proved to be normal.

Case 2. The lungs of a stillborn baby of normal size and weight proved again to be fœtal in character. The developmental arrest had happened very early, which may have been the cause of the intra-uterine death. The lung consisted mainly of mesenchymal tissue.

Comment. The arrest of growth and differentiation of the lung was a local anomaly; other organs were normal.

Case 3. An infant, aged 2½ months, died of diarrhœa and vomiting. The lung was macroscopically normal. Histologically the pulmonary tissue was mainly normal but included small areas of fœtal tissue. Complete histological examination could not, however, be carried out.

Comment. This case proves only that developmental anomalies may occur in small areas and persist for some time.

Case 4. This case deserves special attention because the anomaly was found in an adult.

(*Received for publication October* 5, 1956.)

A married woman, aged 21 years, fell ill and died within twenty-four hours. Food poisoning was supposed to be the cause of death. The body of the woman was well-built and post-mortem examination did not reveal any organic change. However, the histological structure of the lung was so extraordinary that a thorough examination was carried out. It revealed that the air-spaces—*i.e.* the acini—were of the size and differentiation appropriate to very young infants.

Comment. As far as I know the lung of an adult with infantile acini has not been previously recorded.

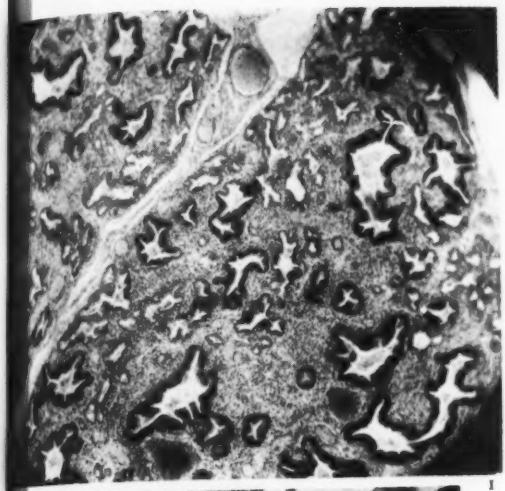
Discussion

It is important to realise at the outset that congenital anomalies of lung tissue can only be understood by comparison with the normal histology of the human lung, especially with the pulmonary structure at various age-periods. It will be unnecessary to discuss here the changes due to age, as the acini of the growing lung have been fully described elsewhere (Engel 1947).

The developmental anomaly in the first three cases is obvious, case 4 requires special consideration. Fig. 3 shows the acinar structure in case 4. It is evident that the acinus as a whole and the alveolar saccules in particular are small and poorly differentiated. Figs. 4 and 5 confirm this. Fig. 4 shows the acinus of an infant, aged 2½ months. Even at this early age the acinus is larger and better differentiated than that of case 4 (Fig. 3). Still more striking is the comparison between Figs. 3 and 5. Both these photographs are taken at the same magnification. Whereas Fig. 3, case 4, represents a medial section through a complete acinus from the terminal bronchiolus to the tips of the alveolar saccules, Fig. 5 taken from the normal lung of a girl, the same age as the woman of case 4, only contains two alveolar saccules arising from a ductus alveolaris. The length of the saccules in case 4 is 0·4 mm. and 2 mm. in the control case; which means that the two saccules are in the ratio of 1 to 5. The saccules of the control case are so long and the alveoli so well marked that it is clear how much the acini of case 4 (Fig. 3) are undersized and underdeveloped. One could speak of " pulmonary infantilism " in case 4.

Developmental anomalies may also occur in the intersitial tissue of the lung. Certain deficiencies, especially of the elastic tissue, have been described elsewhere (Engels, 1947). It is likely that " congenital lobar emphysema " may be due to deficiencies in the interstitial tissue. Holzel *et al.* (1956) have described three cases of this condition which occurred in the neonatal period or in the first few months of life. The distension of the air spaces in their cases (Figs. 1 and 2) is obvious. As this cannot be due to chronic over-expansion as in old-age emphysema, some tissue deficiency, such as weakness of the stabilising elements —viz. elastic fibres, smooth muscle and reticular tissue may have allowed the air spaces to be over-expanded. The deficiency must be considered congenital owing to the very early period of life at which it occurred.

The question whether congenital anomalies of the lung may be the cause of certain pathological conditions such as cystic and/or honeycombed lung cannot be answered with certainty, much more evidence is needed to clarify the point. As the anomalies reported in this paper were observed over a comparatively short period of time, they may not be so rare as has been supposed in the past.



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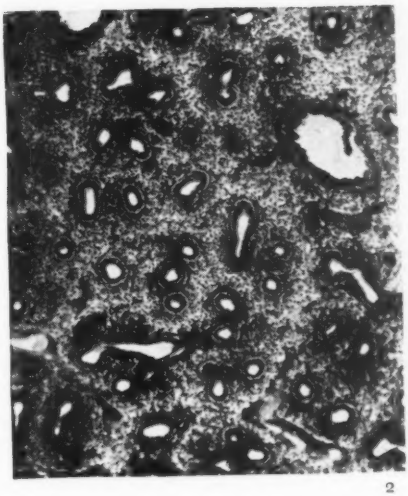

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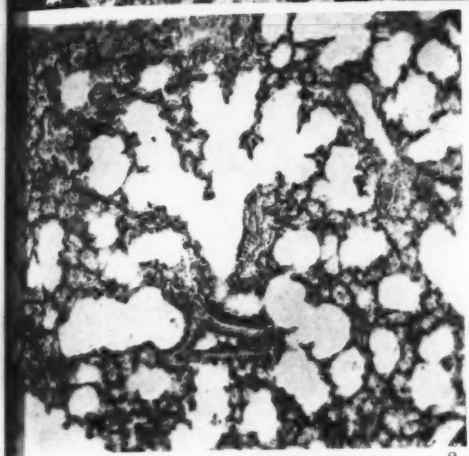

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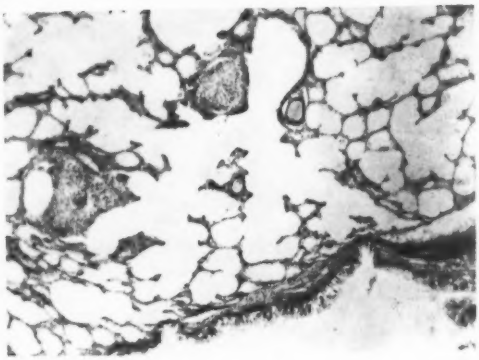

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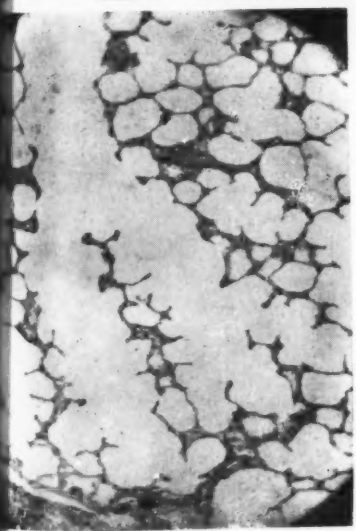

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FIG. 1 (*top left*).—Fœtal lung tissue in a newborn (living) infant. ×35.

FIG. 2 (*top right*).—Fœtal lung tissue in a still-born infant. ×55.

FIG. 3 (*middle left*).—Infantile acinus in an adult woman. ×35.

FIG. 4. (*middle right*).—Acinus of an infant, aged 2½ months. ×35.

FIG. 5 (*bottom left*).—Normal air-saccules of an adult woman. ×35.

Facing p. 58

Summary

Congenital developmental anomalies in the lung can only be observed histologically. They deserve more attention than previously accorded to them in connection with the pathogenesis of cystic and honeycombed lung and congenital lobar emphysema.

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TUBERCULIN SURVEYS IN CUMBERLAND

THEIR EPIDEMIOLOGICAL SIGNIFICANCE AND VALUE

By W. H. P. Minto*

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In 1935 Greenwood wrote: "Without doubt, it is idle to speak of the conquest of tuberculosis; tuberculosis has not been and so far as one can see never will be conquered." The opinion of one of our greatest epidemiologists must not be light-heartedly dismissed, but here surely is a challenge to those of us engaged in the practice of preventive medicine. Can we to-day, with tuberculosis already on the decline, and armed as we are with new and powerful anti-tuberculosis weapons, really accept the thesis that an infectious disease cannot be, if not abolished, at least reduced to the status of a minor health problem by a concentrated attack on its fundamental courses combined with the protection of susceptible groups?

It was with this in mind that, in the autumn of 1954, a tuberculin survey of infant school children was undertaken in selected areas of the county of Cumberland.

The first object was to determine the tuberculin sensitivity of a high proportion of the 5/6-year-old children in the county.

Tuberculin sensitivity is widely regarded as an index of infection with tuberculosis in the community. It follows, therefore, that such a survey should achieve its second aim, which was to provide a reliable picture of the epidemiological pattern of tuberculosis in Cumberland.

The third object of the survey was as a means of case finding among the children and their contacts.

Topography of Cumberland

The county of Cumberland is bounded to the north-west by the Solway Firth. It marches with Dumfriesshire and Roxburghshire in the north. To the west lies the Irish Sea. Its neighbours to the north-east are the counties of Northumberland and Durham and in the south-east Westmorland and Lancashire. The county's greatest length and greatest breadth as the crow flies are 74 and 55 miles respectively and there is a 75-mile coastline.

Much of the county is devoted to agriculture, but at the coast an industrial belt extends from Silloth in the north to Millom in the south and inland south of Workington to the fells.

This industrial belt was prosperous early this century. Coal was mined north of Cleator Moor and under the sea at Whitehaven. Vast deposits of hæmatite iron ore extend south and east of Cleator Moor. Iron and steel industries flourished at Maryport, Workington, Whitehaven, and in the adjacent areas.

* Abridged from a paper presented to the Tuberculosis Society of Scotland at Aberdeen on June 16, 1956.

(*Received for publication July* 12, 1956.)

After the 1914-18 war, however, industrial depression settled upon West Cumberland. Hundreds of young skilled miners left to seek employment elsewhere and, I fear, many of them came home later to die—of tuberculosis.

In 1934 West Cumberland was scheduled as a Distressed Area and at that time there were 13,000 unemployed remaining in the district. The Cumberland Development Council set about a revitalisation of the West Cumberland Development Area and a remarkable industrial renaissance has been achieved in the intervening twenty years.

To-day the basic industries of coal and iron have been brought up to date and there is a great range of varied new light industry which provides work for roughly 7,000 men and 5,000 women. Practically every employable person between the ages of 15 and 65 is in employment. The most recent developments are an atomic energy plant on the coast and a new anhydrite works at Whitehaven.

It would not be fair to say that housing development has lagged behind, for the local authorities have a good housing record, but, as in most parts of the county, a great deal of slum clearance remains to be undertaken. Sanitary services generally are at least up to average national standards.

Administration

The population of the administrative county of Cumberland is 216,100 (Registrar-General estimate mid-1953). Carlisle City, which lies in the geographical county, is a county borough and, as such, forms an entirely separate local government unit. All mention of " Cumberland " in this paper refers to the administrative county.

" Cumberland " comprises two municipal boroughs (Workington and Whitehaven), four urban districts (Maryport, Cockermouth, Keswick and Penrith) and seven rural districts of which one, Ennerdale Rural District, is largely industrial although in a rural setting. For many administrative purposes the County Council and other bodies break the county into " East " and " West " Cumberland.

Epidemiology of Tuberculosis in Cumberland

Consideration of the topography of Cumberland would lead one to anticipate that the incidence of tuberculosis would vary considerably within the county, and indeed the indices of the prevalence of tuberculosis during the period in which the selected age group had been " at risk " suggest that this is so.

It is never easy to find a yardstick for the incidence of tuberculosis in a community and notification (morbidity) rates have been particularly suspect in this direction.

We should consider the trends over the past twenty years in the notification rates for pulmonary and non-pulmonary tuberculosis in the county (Fig. 1).

It has been claimed that this increase in notification is due to improved methods of case findings such as full chest centre facilities and mass radiography surveys, but it must be borne in mind that in this county the increase had started in 1949 before the chest centre facilities (1950 and 1951) and mass radiography (1951) became available.

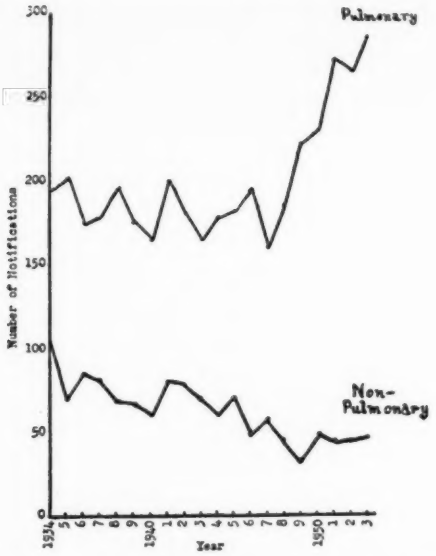

FIG. 1.—Administrative County of Cumberland.
Notifications of Pulmonary and Non-Pulmonary Tuberculosis, 1934-1953.

It might be argued that increased notifications are due to the prolonged survival of chronic fibroid cases with positive sputum who thus cause an increase in the prevalence of infection—one of the problems which might be answered by a tuberculin survey.

On the other hand, one cannot deny the value of mass miniature radiography as a case finding procedure. In its first year of operation (1951) the Unit examined 31,538 persons and detected 114 cases of active, newly discovered tuberculosis. This, I think, constitutes a better epidemiological index than notification rates, and the figures for Cumbrian school children passed through mass miniature radiography in 1952 and 1953 are also revealing (Table I).

TABLE I.—RESULTS OF MASS RADIOGRAPHY—SCHOOL CHILDREN

Year	*School children Examined*	*Active T.B.*	*Per cent.*	*Inactive T.B.*	*Per cent.*
1952 East Cumberland ..	3,069	1	0·03	27	0·9
West Cumberland ..	1,573	1	0·06	16	1·0
1953 East Cumberland ..	3,015	2	0·07	19	0·6
West Cumberland ..	1,692	6	0·35	21	1·2

The figures for mass radiography for 1954 and 1955 once again indicate quite clearly that a higher percentage of both active and inactive cases are found in West than in East Cumberland by this method.


N
W
E
S
E DUMFRIESSHIRE
BORDER R.D.C
Longtown
6·0 %
Brampton
10·5 %
CARLISLE (County Borough)
Silloth
3·5 %
SOLWAY FIRTH
WIGTON R.D.C
Wigton
5·1 %
Aspatria
4·7 %
PENRITH R.D.C
Alston
ALSTON with GARRIGILL R.D.C
Penrith (Urban District)
7·7 %
Maryport (Urban District)
10·8 %
Workington Municipal Borough
6·1 %
Cockermouth (Urban District)
COCKERMOUTH R.D.C
Keswick (Urban District)
12·2 %
11·6 %
Whitehaven Municipal Borough
EGREMONT R.D.C
16·7 %
Seascale
MILLOM R.D.C
Millom
ADMINISTRATIVE COUNTY OF CUMBERLAND
Mean Tuberculosis Mortality 1947 - 1955
Whole County 0·4 Per Thousand
Mean or lower mortality.
Mortality up to 30% above mean
Mortality from 31-60% above mean
Mortality over 60% above mean
Carlisle County Borough
District Council Boundaries
'West Cumberland'/'East Cumberland' Boundary
Figures in Circles are percentage of positive reactors found in the survey
0 1 2 3 4 5 6 7 8 9 10
Scale of Miles

FIG. 2.

It is however probably still true that the death rates are the best guide to the incidence of tuberculosis in an area if they are considered over a period of time.

The death rates per 1,000 population in 1952 and 1953 for East and West Cumberland were:

	1952	1953
East Cumberland	0·08	0·08
West Cumberland	0·27	0·28

The Mean Pulmonary Tuberculosis Mortality, all ages, in Cumberland 1947–53 was 0·4 per 1,000 population. The corresponding figure for all England and Wales for the same period was 0·33 per 1,000 population.

When the distribution of these deaths by district council areas (Fig. 2) is considered, it is found that among the thirteen districts which comprise the county there are only four (all situated in West Cumberland) whose mortality is above the mean (Table II).

TABLE II.—MEAN PUL. T.B. MORTALITY RATES

District	*Mean pul. T.B. mortality* 1947–53	*% above the County Mean* 0·4
Ennerdale Rural District	0·69	72·5
Whitehaven Borough	0·56	40
Workington Borough	0·51	27·5
Maryport Urban District	0·50	25

The districts with the next mean mortality, but below the county mean, are:

District	*Mean pul. T.B. mortality* 1947–53	*% below the County Mean* 0·4
Keswick Urban District	0·34	15
Cockermouth Rural District	0·33	17·5
Penrith Urban District	0·28	30

All the available indices of the prevalence of tuberculosis lead to the conclusion that there is probably a higher incidence of pulmonary tuberculosis in West Cumberland than in East Cumberland, and that there is also a fairly wide variation in incidence through the county.

THE INFANT SURVEY (5/6-YEAR-OLDS)

The Mantoux testing of the infant group commenced in October 1954 and was completed by the end of November.

Eleven areas were chosen, comprising the four largest towns in the administrative county, Workington, Whitehaven, Maryport and Penrith; a group of three smaller towns and adjacent villages, which form the main industrial

community, the Cleator Moor/Frizington/Egremont area of the Ennerdale Rural District; and six small towns in different parts of the county, Keswick, Brampton, Longtown, Wigton, Aspatria and Silloth. The survey would in this way cover all those areas where the incidence of tuberculosis was suspected to be high and where the Mean Mortality rate (1947-53) was known to be higher than the mean for the county as a whole, and also, for purposes of comparison, a number of towns where no undue incidence of tuberculosis was to be expected from the facts available. *It was decided to offer the test to every child who attended school in the selected areas and who was born between September* 1, 1947, *and September* 1, 1949.

The balance of present-day scientific opinion suggests that an intradermal test is likely to be more satisfactory than any of the various jelly tests, in that it is much less prone to give rise to doubtful results. Another important point is that the tests given before and after B.C.G. vaccination must be intradermal (Ministry of Health Circular 22/53), and it was argued that if a test of the same strength (10 I.U.) were used in the autumn survey, the results would be strictly comparable with those of the 13/14-year-old group in the B.C.G. scheme.

The test finally selected was *a Mantoux test involving an intradermal injection in the flexor surface of the forearm, previously cleaned by acetone, of* 0·1 *ml. of a* 1 *in* 1,000 *dilution of standardised Old Tuberculin—that is,* 10 *I.U. The criteria to be adopted for the reading of these tests, after seventy-two hours, was to be that any reaction producing less than* 5 *mm. of induration, with or without erythema, was to be regarded as negative.*

Results of the 5/6-year Group Survey

Table III.—Results of the Survey

Area (1)	*No. of children in age group on rolls* (2)	*No. of consents* (3)	*% of consents* (4)	*No. of completed tests* (5)	*% of children on rolls (2) who completed tests* (6)	*No. Positive* (7)	*% positive of those shown at Col. 5* (8)
Workington	998	792	79	686	69	42	6·1
Whitehaven	985	788	80	665	68	77	11·6
Maryport	544	466	86	400	74	43	10·8
Frizington/Cleator Moor/Egremont ..	650	559	86	450	69	75	16·7
Total all areas West Cumberland	3,177	2,605	82	2,201	69	237	10·8
Silloth	123	98	79	87	71	3	3·5
Aspatria	111	95	86	86	77	4	4·7
Wigton	155	123	80	117	75	6	5·1
Longton	136	98	72	83	61	5	6·0
Penrith	375	303	81	274	73	21	7·7
Brampton	83	67	81	57	69	6	10·5
Keswick	119	109	92	98	82	12	12·2
Total all areas East Cumberland ..	1,102	893	81	802	73	57	7·1
Grand Total	4,279	3,498	82	3,003	70	294	9·8

There were 4,279 children in the 5/6-year-old group on the rolls of the schools in the selected areas. Parental consent to the test was obtained for 3,498 (82 per cent.) of these children. The consent rate is an important factor to be taken into consideration in a survey of this nature. A response of 82 per cent. compares favourably with that obtained in most recent surveys in this country where formal consent was obtained.

The percentages of children on the rolls who completed the test in individual areas are shown at col. 6 of Table III, and it will be noted that, with the exception of Longtown (61 per cent.), they are remarkably constant, both between East and West Cumberland and the individual areas. It can be deduced that the numbers who completed tests in each area are sufficient to provide a representative sample suitable for comparison.

Two hundred and ninety-four positive reactors (9·8 per cent.) were found. Of these 237 (10·8 per cent.) were in West Cumberland and 57 (7·1 per cent.) in East Cumberland. There was a very wide variation in the incidence of positive reactors in the individual areas varying from 3·5 per cent. in the Silloth area to 16·7 per cent. in the Frizington/Cleator Moor/Egremont area.

In East Cumberland 73 per cent. of the children on the rolls completed tests and 7·1 per cent. were found to be positive reactors, while in West Cumberland of the 69 per cent. who completed tests, 10·8 per cent. were positive. It is true to say, therefore, that the incidence of tuberculous infection in the age group tested, as indicated by the tuberculin reaction, shows a similar relationship between East and West Cumberland as that evidenced by the mortality rates and mass radiography surveys in 1952 and 1953, and is generally in accordance with what is known of the natural history of tuberculosis in Cumberland.

Effect of B.C.G. Vaccination on the Results

In a detailed study of the literature of recent surveys I can find no reference to the possible effect which the inclusion of children who have been given B.C.G. vaccination as contacts may have had on the results. It could, of course, be argued that a negative contact would be likely to have become naturally positive if B.C.G. had not been administered. This argument may well be valid in an unknown proportion of cases at least, but in view of the fact that B.C.G. has been offered to all tuberculin negative contacts of known cases of tuberculosis in East Cumberland since 1950 and in West Cumberland since 1951, it was felt that the influence, if any, of this procedure on the results should be determined.

The findings were of some interest. In East Cumberland none of the positive reactors were found to have had B.C.G. vaccination. The only explanation of this would seem to be that the parents of these children who had had B.C.G., having a better understanding of the implications of the test offered, withheld consent. In West Cumberland, on the other hand, 29 children, whose reaction to the tuberculin test was positive, were found to have had B.C.G. vaccination. This means that if all these children had not had B.C.G. and had remained negative—an unlikely event—9·5 per cent. instead of 10·8 per cent. would have been found positive in West Cumberland in comparison with 7·1 per cent. in East Cumberland. Even this would not alter

the comparisons to be discussed below. The distribution of post-B.C.G. positive reactors in the individual areas was Frizington/Cleator Moor/Egremont —12; Workington—9; Maryport—6; Whitehaven—2. Broadly speaking, this might narrow the gap between the Ennerdale area and Whitehaven and widen that between Workington and the remainder of West Cumberland, but the relationship of the four areas cannot have been substantially altered by B.C.G. vaccination.

This little investigation, while it does not radically alter the findings in the present survey, indicates that the factor should be taken into account in future surveys, particularly in view of the fact that B.C.G. vaccination is being increasingly offered to susceptible contacts, and I understand that the definition of contact in this respect is, probably rightly, becoming more elastic.

The 13-year-old Group Survey

In 1955, the same 1 in 1,000 Mantoux test, followed by B.C.G. vaccination where necessary, was offered to all school children in their fourteenth year. This provided an indication of the extent and distribution of tuberculinisation in the 13-year-old group.

Explanatory letters were sent to the parents of all the 2,802 children in the age group and the acceptance rate was 80 per cent., which, allowing for the fact that some of the non-acceptors would have had B.C.G. under the contact scheme, may be considered a fairly satisfactory response.

Tests were completed on 2,190 children, which represents 78·5 per cent. of the school child population in respect of whom the offer was made. Of these, 667 (30 per cent.) gave a " positive " reaction.

Table IV.—Results of pre-B.C.G. Mantoux Testing and Entrant Survey

Area	*13-year-old children (born 1941) Tested 1955*			*Entrants (5/6-year-old) Tested autumn 1954*		
	No. tested	*No. positive*	*% positive*	*No. tested*	*No. positive*	*% positive*
Alston	26	3	11·5			
Border	222	40	18	140	11	7·8
Wigton	224	62	27·7	290	13	4·5
Keswick	101	10	9·9	98	12	12·2
Penrith U.D.	133	30	22·6	274	21	7·7
Penrith R.D.	60	9	15			
Total—East Cumberland	766	154	20·1	802	57	7·1
Maryport	119	42	35·2	400	43	10·8
Workington	414	141	34·1	686	42	6·1
Whitehaven	414	145	35	665	77	11·6
Ennerdale R.D.	209	81	38·8	450	75	16·7
Cockermouth	136	48	35·3			
Millom	132	56	42·4			
Total—West Cumberland	1,424	513	36	2,201	237	10·8
Grand Total	2,190	667	30·4	3,003	294	9·8

Table IV shows the position in the different sanitary districts and allows comparison with the situation affecting the 5/6-year-old group in the first survey.

Epidemiological Significance of the Results

It is proposed to consider the results of the 5/6-year survey in the selected areas and to comment on the results for the 13-year group when they affect the conclusions which have been drawn.

East Cumberland

In East Cumberland the incidence of positive reactors is extremely low, in comparison with other recent surveys, for what is a predominantly rural agricultural area. Cumberland has been in the past a stock-raising county, with the result that virtually no milking cows are imported into the county. This, combined with the energetic policy which has led to the declaration of an eradication area, must be an important factor in the low incidence of bovine tuberculosis over the last eight years or so which these findings seem to confirm.

The numbers tested are relatively small, but the figures of positive reactors in the coastal estuarine region of the Solway and to the north-west of the Carlisle plain (*Silloth*, *Aspatria* and *Wigton*) are unusually low. The percentage positive in the 13-year group in this district (Wigton), on the other hand, is the highest in East Cumberland. It could be argued that many of this group acquired their infection from milk in the bad old days of their youth, but we must not overlook the fact that cases of active pulmonary tuberculosis in this age group have been found in one of the large secondary schools here. The situation here seems to merit more comprehensive and more local surveys, and a careful follow-up of the original 5/6-year group annually or biennially.

The main point of interest in *Longtown*, where the low consent rate had been attributed to a high proportion of refusals from the mid-European workers' camp nearby, is that four of the five positive reactors were children of Polish descent. This indicates that special measures should be taken with regard to the investigation of this community.

Following upon the survey at *Brampton* (10·5 per cent.), where a new active case of non-pulmonary tuberculosis was found, three cases of open tuberculosis in cattle were discovered, one involving tuberculosis of the udder. Bovine infection may well have been a relevant local factor here.

Penrith is of some importance, as not only has it the largest population, but on the findings of the surveys may be taken to be a town typical of East Cumberland (7·7 per cent. positive reactors) and may be usefully compared with the typical West Cumberland town of *Maryport*.

The relationship of percentages positive in the two age groups are almost identical for Maryport and Penrith. In each town for every positive reactor in the 5/6-year group there are three positive reactors at 13 years of age. In other words, in both Maryport and Penrith a child aged 13 years is three times more likely to have contracted a tuberculous infection than a 6-year-old, but the chance of infection at either age is greater in Maryport.

In the "entrant" survey, *Keswick* showed a higher incidence (12·2 per cent.) than was to be expected relative to the other areas; in fact, this small,

pleasant town showed the second highest result in the county. It should be noted however that, although below the mean mortality rate for the county Keswick did come next to the industrial areas in West Cumberland in that respect.

It was surprising to find that only 9·9 per cent. of the 13-year-old children showed " positive " reactions—the lowest figure for the county. There is a grammar school which takes boarders, and when the 101 children tested are divided into those resident in Keswick and those whose normal residence is outside, we find 46 local residents of whom 7 (15·2 per cent.) were " positive."

The problem has not been solved and will require further local investigation, but some factors which may have a bearing on the findings can be discussed here.

Keswick is the natural centre of the English Lake District, which has often been likened to a miniature Switzerland. It must be a favourite choice for long- or short-term retirement by those whose health is suffering from the strain of life in the larger cities and industrial centres. It is a most attractive residential town with a cultural background and those who retire here permanently are as a rule well-to-do. My theory—and it first came to my notice under similar circumstances during my tenure of office as Medical Officer of Health to a north Cornish seaside resort—is that those people, many of whom are elderly, who suffer from indefinite respiratory complaints and even known tuberculosis will come to such an area to recuperate or to retire permanently in the not unreasonable hope that their health will benefit. There can be, it will be appreciated, under these circumstances an extreme reluctance on the part of both patient and practitioner to notify or even to confirm the diagnosis. A sizeable reservoir of unknown infection is thus built up, which may not even be reflected in mortality rates and which constitutes an exceptional hazard to a relatively unsalted population.

Another contributory factor is the overcrowding which takes place in the summer months—at times of conventions this becomes extreme—even in residential areas. This factor is often lost sight of in housing surveys, which are almost invariably undertaken out of the " season."

Infection in a school (presumably teaching staff are as likely as others to find appointments in a " healthy area ") must be considered. Every effort is made to induce school teachers and food handlers to attend mass radiography sessions voluntarily, but I fear the attendance is by no means 100 per cent. and we have no powers of compulsion. It is of interest that here one " positive " child's mother, who is employed in the School Meals Service, had three small tuberculous foci at the left apex and is now under observation at the chest clinic.

A sanatorium is situated near Keswick, but I think infection due to patients visiting the town, although a remote possibility, is unlikely to be an important factor. The numbers engaged in a small granite industry near by could not materially affect the issue.

The history of milk supplies in Keswick during the period in which these children have been at risk is good and compares favourably with the rest of the county. On pursuing my enquiries a little further, I find that at the height of the season the milk supply not infrequently fails to satisfy the demand and an ungraded bulk supply is sent in from outside Cumberland. So we have again

the same story, that while it is admitted that for infection the tubercle bacillus *must* be present—be it human or bovine—the seed may well be brought in from outside an area and fall on fertile soil.

In West Cumberland the highest incidence was found in what has always been regarded as the " black spot " for tuberculosis—Ennerdale Rural District (*Frizington/Cleator Moor/Egemont area*): 16·7 per cent. of the 5/6-year-old children tested were found to be positive reactors.

When the 13-year-old children were tested it was found that 38·8 per cent. gave a positive reaction. These figures were broken down further and it was found that the percentage positive in the Frizington/Cleator Moor/Egremont area was 42 per cent. and higher still for the children in the Roman Catholic schools.

It has been known for many years that the Ennerdale Rural District has had a much higher death rate from pulmonary tuberculosis than any other part of the county. The chief industry is still hæmatite iron ore mining, and I believe the bulk of iron worked elsewhere in this country is iron stone, which does not give off a fine dust when drilled as does hæmatite. Prior to 1914 the ore was drilled by hand and jumper, but increasing mechanisation not only contributed to unemployment but also in its early days increased the dust in the air of the mines, thus increasing the risk of silicosis, a known precursor of tuberculosis.

As the iron ore industry developed from 1860 onwards, the population rapidly increased. Irish immigrants flocked to the mines and also the linen thread mills, where work ceased in 1926. While it is improbable that the Irish ever actually outnumbered the native Cumbrian population, it is certain that a substantial proportion of the population of the area was and still is of Irish extraction. There was also an important, although smaller, influx of Cornish miners at the end of the last century, resulting from the rapid decline of the tin mining industry in Cornwall. These Cornish miners seem to be particularly susceptible to tuberculosis, and the effect of their arrival and exposure to silica in appalling conditions in the mines should not be underestimated.

At the turn of the century, iron ore miners in Cumberland began to emigrate to the South African goldfields and to Canada and the Americas. This emigration continued to be a feature of the period between the wars and was encouraged by the industrial depression. Many died abroad of miner's phthisis and many came home to die, or worse, to work in ill-ventilated mines, bringing with them the seed of tuberculosis to fall on soil made fertile by racial factors, poverty, poor housing and industrial depression.

This then, briefly, is the background of the Frizington/Cleator Moor/Egremont area. When we add the fact that it is here that we find the highest proportion of defaulters from chest clinic attendance, self discharges from sanatoria and refusals to accept in-patient vacancies, it becomes clear that this area may require the application of quite different methods of tuberculosis control from the rest of the county.

The *Whitehaven* incidence of 11·6 per cent. and 35 per cent. for the 13-year-olds is in accordance with what was previously known of the incidence of tuberculosis in the area. A striking feature in the 5/6-year survey which should be elucidated is that there is a large modern infant school on each of two housing estates whose populations are in the region of 4,000. The schools are of similar

size and the one on the new estate which is still in the process of completion yields 9 per cent. positive reactors, while the percentage positive on the older estate is 24 per cent. The corporation's policy of rehousing tuberculous applicants has not altered, and one wonders if this is yet another instance supporting M'Gonigle's suggestion that disguised poverty on housing estates contributes to increased tuberculosis morbidity and infant mortality rates—the inhabitants of the older estate having been more affected by the depression. To me, a more attractive theory is that children of families newly housed are prone to be found next door, and a policy which gives priority to the rehousing of tubercular persons may lead inadvertently to the infection by neighbourliness of non-tubercular families. At any rate, here are two largely closed communities in one town where case finding and subsequent investigation may provide an answer.

It is rather surprising in the light of mortality rates to find *Workington* with an incidence (6·1 per cent.) just over half that of her twin borough Whitehaven. A number of factors may be at work here: the Workington population is of predominantly Cumbrian stock and the town did not suffer from unemployment in the depression so much as adjacent areas, due to continual although reduced work at the port and iron works. The main factor, I think, is the attitude of the people (there may be a racial element here) to tuberculosis. In Workington there are fewer defaulters from the chest clinic attendance, self discharges from sanatoria and so on. The number of Workington children found " positive " in the survey, too, gives one reason to hope that the apparently low incidence of infection may be a real one and that conditions here are yielding to the measures of tuberculosis control which have been introduced.

The results of the Mantoux testing prior to B.C.G. vaccination in the 13-year-old group here show a percentage of 34·1 per cent. positive reactors, which corresponds more closely to the expected incidence. This, I would contend, supports the view that the future for tuberculosis control in Workington promises well.

The Surveys as a Guide to Future Policy

It should now be possible to discuss the policy which is likely to employ the available resources to the best advantage in an attempt to bring nearer the day when tuberculosis will become an unimportant disease in Cumberland.

It should be safe to say that before long no Cumbrian baby is likely to be infected with bovine tuberculosis within the county as he grows up. We are now concerned therefore largely with his protection from human tuberculosis.

The obvious methods of approach to this problem are the detection and treatment of these " open " cases and the protection of susceptible contacts, using the term " contact " in its widest sense.

Different areas will require different treatment if the best results are to be obtained. Speaking very generally, the population of Ennerdale Rural District, for instance, is notoriously unwilling to submit itself to investigation with regard to tuberculosis and also to treatment when this is indicated, particularly if admission to sanatorium is involved. It may be that many have experienced in their families the sorrow and horror of the terminal stages of phthisis in the

past and the impression left dies hard. Health education regarding tuberculosis will be an uphill task here and compulsion as used in some countries is contrary to the British way of life. The " entrant " survey shows that at least 16·7 per cent. of the school children have or have had a tuberculous infection before reaching the age of 7. Forty per cent., perhaps more, of the 13-year-old Ennerdale children are positive reactors. It might be desirable to seek approval to offer B.C.G. vaccination to all tuberculin negative school entrants (5-year-olds) and simultaneously to offer mass radiography examination to the contacts of the positive reactors. It would seem almost criminal, in view of the situation described, to carry out another tuberculin survey of school entrants in this area without offering B.C.G. Mantoux tests and B.C.G. would still be offered to 13-year-old children to ensure their tuberculin conversion before they leave school and enter often dangerous industry. When those who had B.C.G. at 5 reached 13, those who had reverted would be offered revaccination. If it is held that the duration of protection from B.C.G. is only up to five years, this scheme should still cover the " danger years " adequately. In this area, because of the peculiar circumstances, it might be desirable to offer B.C.G. vaccination to babies at the welfare centres to minimise the risk of meningitis, even though segregation would be impracticable.

In Workington, on the other hand, where the population has been very co-operative in this respect, simpler and more orthodox measures would be as likely to produce the desired effect. The other areas should be considered each on its merits; in Keswick, for example, a public appeal on the intellectual plane might well be of considerable value.

I have tried to emphasise above all that the methods of tuberculosis control should not be too rigidly laid down at any level; they must be adapted to suit local conditions within a county, or possibly a city, and one must add that these local conditions must be kept constantly under watchful review so that the methods can be changed to meet altered conditions.

Conclusions

The figures for the different areas, with exceptions which have been discussed, demonstrate a significant variation which corresponds closely to that shown by the mortality rates from pulmonary tuberculosis for the period during which this age group was " at risk," and other indices of human tuberculous infection. It is, therefore, concluded that the tuberculin test used is a reasonably reliable index of the incidence of human tuberculous infection in this age group in Cumberland.

From a study of other surveys—and it is surprising that there is no record in the literature of similar local surveys in an English county—it can be deduced that tuberculous infection as indicated by the tuberculin conversion rate is on the decline. If the tuberculin test is a reliable index of tuberculous infection it should follow that the number of sputum-positive cases in the community is decreasing. This statement is made with some reserve, having regard to the high incidence of bovine tuberculosis in some of the other areas surveyed and in the light of the tests used which may, by covering both high and low grade tuberculin sensitivity, have revealed an unduly large number of positive

reactors, thus failing to provide a true index of tuberculous infection in the community.

The most important conclusion to be drawn from these surveys is that there is a need for a large number of surveys of this type in order that an accurate knowledge of the incidence of tuberculous infection *locally* may be obtained. It is well known that the prevalence of infection varies considerably in different localities, but it is not, I think, appreciated just how wide these variations, as demonstrated by the Cumberland results, can be in adjoining districts of counties and even towns. This is an observation of more than academic interest, for it is only with a detailed knowledge of the prevalence and the attack rate at different ages that it can be possible to decide which are the anti-tuberculosis measures to be most usefully employed in any area. For instance, it is only in this way that the most susceptible group to whom B.C.G. vaccination should be offered in each locality can be accurately determined.

It is not claimed that these surveys are in any way an end in themselves. They constitute, however, a new approach to the tuberculosis problem in Cumberland and mark the start of an investigation which will involve further tuberculin testing surveys of the same and different age groups, thus making available in the course of time a considerable volume of new local information relating to the natural history of tuberculous infection in the county. This essential knowledge should facilitate the optimum deployment of the forces at our disposal in a campaign whose ultimate goal must be the eradication of human as well as bovine tuberculosis.

My thanks are due to the consultant chest physicians, Dr. Hugh Morton and Dr. R. Hambridge, and their assistants for their co-operation in the case finding and their ready acceptance of the additional clerical work involved; to Dr. J. Steven Faulds, for much information about the history of hæmatite ore mining in West Cumberland and for the preparation of the Old Tuberculin; to the District Medical Officers of Health/Assistant County Medical Officers.

Above all, I am indebted to Dr. Kenneth Fraser, formerly County Medical Officer for Cumberland, for his permission to undertake the surveys and for his invaluable guidance and encouragement throughout.

I should add that the opinions expressed in this paper are my own and must not be taken to represent those of the Cumberland County Council.

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TUBERCULIN SENSITISATION IN MAN

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Since the beginning of the century a considerable amount of evidence has accumulated to show that the small amounts of tuberculin used in skin testing may significantly enhance the response to subsequent tuberculin. Within a few months of his first publication of the tuberculin scratch test, von Pirquet (1907) described how repetition of the test in a tuberculin-positive subject may lead to an increased reaction, and noted that this change occurs more readily and more constantly in the absence of active tuberculosis. Other workers have shown that the site of previous tuberculin injections may show fresh activity, or existing responses show an increase in size, as a result of the intravenous injection of tuberculin (Klingmuller, 1903), as the result of lymphatic carriage of tuberculin from one response to another (White and van Norman, 1910), or simply following further doses of intracutaneous tuberculin (White and Graham, 1909; Holmes, 1914; Westwater, 1934). In addition, there are a small number of observations to show that, once a positive response has been obtained, reaction may be elicited to a smaller, and previously ineffective, dose of tuberculin (Bass, 1918) and that the response to the second of two identical doses, separated by a larger dose, may be modified in a special way (Mantoux, 1910).

The changes described by von Pirquet in the response to succeeding doses of tuberculin have been repeatedly confirmed for all the skin tests at one time or other in common use (Cohn, 1907; Levy, 1908; Ellermann and Erlandsen, 1909; Grundt, 1913; Bjornstad, 1941; Honkanen, 1944), and the possibility of using failure to sensitise in this way as a diagnostic or prognostic index in tuberculosis has been frequently discussed (Kögel, 1912; Grundt, 1913; Honkanen, 1944). In contrast, the other changes—reaction to a previously ineffective dose of tuberculin, and the reappearance of activity at a faded site—have received little attention. Partly because of this neglect, partly because following sensitisation the responses may resemble closely those previously described in certain cases of tuberculosis (O'Grady, 1956), and partly because there is again a difference in behaviour in the presence or absence of active tuberculosis, these changes seemed to warrant further study.

Methods and Materials

A series of patients were Mantoux tested at two- to three-day intervals with ten-fold decreasing dilutions of old tuberculin, beginning with a dilution of 1 : 10,000, until a dose was given which produced, after forty-eight hours, easily palpable induration not less than 6 mm. in diameter. Greater doses than the 1 : 100 dilution were not given. The tests were conducted, read by

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two independent observers, and the responses classified as "normal" or "tuberculous" as previously described (O'Grady, 1956).

In the present paper the term *non-tuberculous* is used both for those patients suffering from diseases other than tuberculosis and for healthy subjects. The term *tuberculous* covers both patients suffering from clinically active parenchymatous pulmonary disease and those with primary pleural effusions. With the specific exception of the Mantoux-negative group referred to, all the subjects, both non-tuberculous and tuberculous, were tuberculin positive. Patients positive to the 1 : 10,000 (1 t.u.) dilution were used in a study of the response to repetition of the same dose, and are excluded from the present consideration.

The patients positive to 10 t.u. were reinoculated, on a random basis, two to nine days after the 10 t.u. dose, with 1 t.u. Those positive to 100 t.u. were inoculated two to three days later with 10 t.u. and two or three days after that with 1 t.u. In addition, a group of non-tuberculous patients failing to react to 100 t.u. were similarly reinoculated with 10 t.u. and then 1 t.u. at two or three day intervals.

Results

The results are based on 162 Mantoux-positive and 25 non-tuberculous Mantoux-negative patients. In the positive group, 137 reacted to a dilution of 1 : 1,000 (10 t.u.), 44 being non-tuberculous and 93 tuberculous, and 25 to a dilution of 1 : 100 (100 t.u.), 8 being non-tuberculous and 17 tuberculous.

Group positive to 10 t.u.

The patients positive to 10 t.u. and reinoculated with 1 t.u. have been divided into three groups:

1. Non-tuberculous subjects. In keeping with the previously reported series, all these patients showed "normal" responses.
2. Tuberculous subjects who also showed "normal" responses.
3. Tuberculous subjects who showed the attenuated "tuberculous" response previously described as characteristic of activity.

Two related changes can be recognised in certain of these patients:

1. Coincident with the development of the reaction to the 10 t.u. dose, a reaction develops at the site of the previously ineffective 1 t.u. dose. This has been called *activation* (this includes, of course, both reactivation, where there has been a previous reaction, and the appearance of a reaction for the first time at the site of an ineffective injection).
2. Following the development of a positive reaction to 10 t.u., the injection of a second dose of 1 t.u., previously ineffective, gives rise to a reaction. This has been called *sensitisation*.

The development and relation between these changes in two representative cases is illustrated in Fig. 1.

In a number of cases the injection of the first dose of 1 t.u. produced no reaction at all. In these, the development of any measurable response at the site of the first or in response to the second 1 t.u. dose has been regarded as evidence of activation and sensitisation respectively. Where a small response (but less than positive by the present criteria) was obtained to the first injection

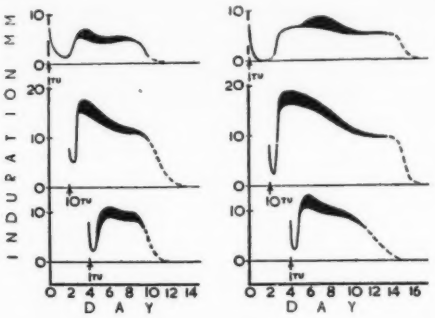

FIG. 1.—Development of induration at the site of previous 1 t.u. injection and in response to subsequent 1 t.u. following normal response to 10 t.u. in (left) normal and (right) tuberculous patient.

The lower edge of the curve shows the diameter, and the thickness of the line the depth of induration.

of 1 t.u., activation has been defined as being present when an increase of at least 30 per cent. occurred in the size of the reaction. Correspondingly, sensitisation has been defined as being present when a response was obtained to the second 1 t.u. dose at least 30 per cent. greater than that to the first.

The numbers of patients showing these changes are given in Table I. A comparison of the size of the reaction to 1 t.u. before and after the effective dose, as a percentage of the maximal size of the reaction to 10 t.u. in the group showing sensitisation, is shown in Table II. The overall experimental error of the method has been regarded as about 30 per cent. and the responses have therefore been divided into three groups: 0–30 per cent., 35–65 per cent. and 70 per cent. and more of the 10 t.u. reaction size. In all groups the number of patients showing sensitisation increases with increasing interval between the 10 t.u. and second 1 t.u. dose (Table I). The relative increase is greater in the tuberculous than in the non-tuberculous group.

In some cases an important change occurred in the type of reaction when patients were retested with 1 t.u. All these patients responded with easily palpable induration to 10 t.u. and on the basis of this response were divided into those giving "normal" and those giving "tuberculous" responses. Neither of the inoculations of 1 t.u., however, necessarily gave rise to induration, which was more than "very shallow," and in some, therefore, the type of the second response could not be assessed, depending as it does on the duration of induration of more than "very shallow" depth. The type of response on retesting with 1 t.u. in those cases in which it could be assessed is shown in Table IV.

Group positive to 100 *t.u.*

In the patients positive to 100 t.u. the difficulty of assessing the type of response recurs. Patients giving only "very shallow" induration to 1 and 10 t.u. were reinoculated with 100 t.u.; but "very shallow" induration in response to this dose was accepted as a positive result if it exceeded 10 mm. in diameter. Larger doses were not given. Since the type of response cannot

always be determined in these cases, therefore, the patients have been divided simply into those with and those without evidence of active tuberculosis. The relation in size of the responses before and after sensitisation is shown in Table IV. The maximal average diameter of the responses to 1 and 10 t.u. before and after the effective 100 t.u. dose are expressed as percentages of the maximal diameter of the 100 t.u. response. Activation affecting the site of both the 1 t.u. and 10 t.u. doses occurred in 3 of these patients, and affecting the 1 t.u. site only in a further 2, 1 in each group being tuberculous. Sensitisation was seen in 6 of the 8 non-tuberculous patients and in 5 of the 17 tuberculous. Usually

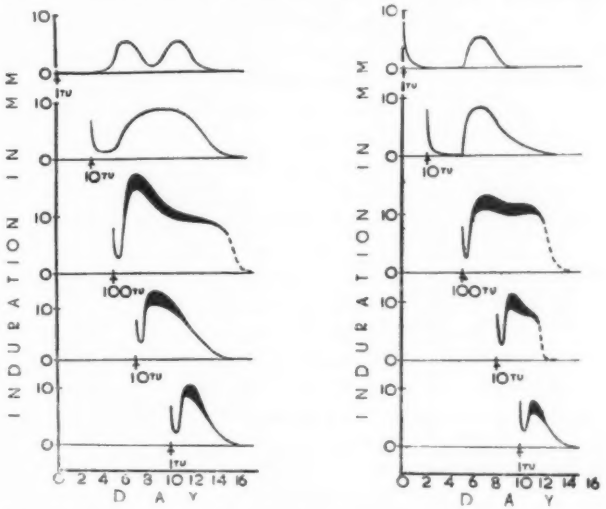

FIG. 2.—Full serial sensitisation and activation in two patients (left) normal and (right) tuberculous, initially negative to 1 and 10 t.u.

The lower edge of the curve shows the diameter, and the thickness of the line the depth of induration.

sensitisation occurred only to the 10 t.u. dose, but in 1 of the non-tuberculous and 1 of the tuberculous sensitisation was obtained to the 1 t.u. dose in addition (Fig. 2). In the tuberculous group, a reduced response was obtained in 4 cases to the second 10 t.u. dose and in 1 case to both the 10 t.u. and 1 t.u. dose (Table IV).

Mantoux-negative Group

No response was obtained on repeated testing of those negative to 100 t.u.

Discussion

When an effective dose of tuberculin is given, two changes may occur: a reaction at the site of previously ineffective doses of tuberculin, *activation*, and a reaction to subsequent repetition of such doses, *sensitisation*. These changes coincide in time with one another and with the development of the response to the effective dose. In those suffering from active tuberculosis these changes

can be elicited less commonly, and they are rarer still in those subjects who exhibit a " tuberculous " response to the effective dose of tuberculin. With increasing interval between the effective dose and subsequent small dose the number of patients showing sensitisation increases.

The coincidence in time of the processes of activation and sensitisation makes it appear that they share the same mechanism, the first involving residual tuberculin at faded sites and the second tuberculin freshly inoculated. All the available evidence suggests that these changes are dependent upon circulating tuberculin, in the present experiments derived from cutaneous sites of injection, some of which is distributed to the skin. Its effects there may be explained either by simple summation of tuberculin dosage or it may induce an actual increase in sensitivity. In the present state of our knowledge the value of attempting to distinguish between direct and indirect tuberculin effects may be questioned, but the possibility of an actual change in the responsiveness of the body is clearly an important one.

In serial testing, as has been pointed out by Johnston, Howard and Maroney (1934), it is common to find an abrupt change in responsiveness on reaching the effective dose, and it is possible therefore that against a background of previously or subsequently injected tuberculin a small dose, by itself insufficient to elicit a response, may raise the local concentration above the threshold. Although the prolonged duration of sensitisation may be explained by the known persistence of tuberculin in the skin, however, it is more difficult to explain on this basis the comparatively slow development of sensitisation. Even the known persistence of tuberculin refers to skin inoculation sites; the rate of uptake and fixation of circulating tuberculin by normal skin is unknown. In common with most other observers it has been found that, following a dose of tuberculin, sensitivity increases for a week or more, while it appears that loss of aqueous antigens from skin sites occurs very rapidly (Talmage and Dixon, 1953) and that fixation of tuberculin is complete within a few hours (Pepys, 1955).

The alternative explanation is that an effective dose of tuberculin initiates a rise in the level of sensitivity. This rise accompanies and is indeed indicated by the response to the effective dose, and it is at this elevated level of sensitivity that the response to smaller doses, recognised in activation and sensitisation, occurs. It appears that the level of sensitivity is usually maximally affected by the administration of a single effective dose, but further rise in the level may sometimes follow the injection of subsequent doses of tuberculin. Fig. 1(*r*) illustrates such a case in which increase in depth, but not in diameter, of the already activated 1 t.u. response coincides with the second 1 t.u. reaction. The double peak in the first 1 t.u. reaction in Fig. 2(*l*) results from the same change.

If this explanation is correct, and it does not exclude some dependence on tuberculin dosage, the rôle of tuberculin in eliciting these responses must be a double one, acting both as a stimulator and at the same time as an indicator of sensitivity. If the injection of an effective dose of tuberculin produces an increase in sensitivity, the injected site itself is unlikely to be exempt. The degree or level of sensitivity which is indicated, therefore, is not that prevailing before the test was instituted but that resulting from sensitisation.

A further interesting change is shortening of the duration of the later responses and a change in form of the reactions (Table III and Fig. 2), possibly identical with that described by Wolff-Eisner* (1908) and the " forme fugace " of Mantoux (1910). Responses of this kind in which easily palpable induration lasts for a very short period (three days or less) have previously been noted as characteristic of the presence of active tuberculosis when occurring in response to the first effective dose of tuberculin (O'Grady, 1956). In those subjects giving " normal " responses to the first effective dose of tuberculin, following sensitisation responses of the " tuberculous " type may continue to be elicited after the subsidence of the sensitising reaction, but it is not known whether this change persists as long as sensitisation itself.

In the group of patients giving a " tuberculous " response to the first effective dose of tuberculin both sensitisation and activation were rare, and where a response to a previously ineffective dose of tuberculin could be obtained, it was always of the " tuberculous " type. In the patients negative to 100 t.u. no change could be elicited to subsequent doses of tuberculin, a finding in keeping with long experience that tuberculin type sensitivity cannot be established in the absence of anatomical tubercles by repeated tuberculin injections (Wolff-Eisner, 1908; Bass, 1918).

All these findings taken together suggest that the " tuberculous " response is the result of recent antigenic stimulation, either from an existing lesion or tuberculin inoculation. In certain tuberculous patients the level of intrinsic antigenic stimulation is high and not increased by small doses of tuberculin. Such a state of stimulation, in which further sensitisation and activation are induced with difficulty, is characterised by a response of the " tuberculous " type. In the non-tuberculous, tuberculin-positive subject, on the other hand, the level of intrinsic stimulation is low and small quantities of tuberculin may as a result make a significant contribution to the total antigenic stimulus with increase in tuberculin sensitivity. If the sensitivity is sufficiently changed, the form of the response to small doses of tuberculin becomes of the " tuberculous " type. In tuberculous patients in whom the " normal " response is initially obtained, it is to be expected that conversion to the " tuberculous " response would occur more readily and sensitisation less readily than in non-tuberculous subjects. The present findings show this to be so, and it is possible that the relative frequency of " tuberculous " responses to the 10 t.u. dose (O'Grady, 1956) is in part dependent upon the sensitising effect of the previous 1 t.u. injection.

It has been shown in tuberculin testing cattle that there is a logarithmic relationship between the depth of induration on Mantoux testing and the dose of tuberculin (Wadley, 1949). A similar relationship between diameter of the indurated plaque and the dose of tuberculin has been observed in the guinea-pig by Long and Miles (1950). It is important in the present connection to point out that in man a simple dose-response relationship, described by von Pirquet (1907; 1910), White and Graham (1909), and others, applies only in certain

* Since the previous work was published, further study of the literature has revealed that Wolff-Eisner and Teichmann (1908) described von Pirquet responses in the presence and absence of active tuberculosis closely corresponding with the " tuberculous " and " normal " Mantoux patterns.

circumstances. In carrying out serial as distinct from simultaneous tuberculin testing where a number of widely differing doses are given at the same time, it is common to obtain no response to the inoculation of 1 t.u. followed by a normal response to 10 t.u., or even no response to both these doses followed by a normal response, often 10 mm. or more in diameter, to 100 t.u. In these circumstances it is clear that there can be no logarithmic or other simple relationship in the dose responses. Following an effective dose, however, sensitisation occurs and reactions may be obtained to small doses which may be related in size to the effective reaction. The relationships in size between the reactions before and after sensitisation are shown in Tables II and IV. In the tuberculous groups there is of course little change, but in the non-tuberculous groups a large number of results move from the 0–30 per cent. to the 35–60 per cent. group. There is as well, however, a greater increase in size, so that the second 1 t.u. dose produces some reactions almost as great in size as those resulting from 10 t.u. These possibly represent the maximal reaction to a given dose in skin pre-sensitised by the previous inoculation, as distinct from the reaction to concurrent sensitisation occurring with the effective dose.

If, in contrast, in determining the level of sensitivity all doses are given at once (Atstatt, 1927), provided an effective dose is included, or possibly provided the total dose given is effective, then alteration of the level affects all the doses similarly and a relationship between the responses may be demonstrated. Elevation of the sensitivity level may also explain another important difference between simultaneous and serial testing. When simultaneous testing is carried out reactions can be obtained to very small doses of tuberculin which by themselves are quite ineffective (sometimes a reaction of 10 mm. may be obtained in response to a dilution of 1 : 10 million). These doses are certainly very much less than those to which reaction may be obtained in equivalent circumstances to serial doses of tuberculin (for example, Hart, 1932, found about 15 per cent. and Lichtenstein, 1934, about 24 per cent. of their tuberculin-positive subjects negative to 1 t.u.), and are also considerably less than those to which serial sensitisation can be obtained. One practical consequence of this is worth noting. In comparative trials of methods of tuberculin testing, the total dose of tuberculin given may sensitise the subjects so that responses are obtained even to those methods in which the amount of antigen introduced is inadequate for normal testing purposes.

Summary

1. The intradermal injection of an effective dose of tuberculin in a tuberculin-positive subject may result in two changes:

(*a*) Coincident with the response to the effective dose, a response may develop at the site of a previous ineffective dose of tuberculin. This change has been called *activation.*

(*b*) Following the effective dose, a response may be obtained on repetition of a previously ineffective dose. This change has been called *sensitisation.*

2. These changes coincide in time with one another and with the development of the response to the effective dose.

3. Both these changes occur less commonly in those suffering from active

tuberculosis and are rarer still in those giving a " tuberculous " response to the effective dose. There is, however, no absolute relationship between failure to exhibit these changes and activity.

4. With increasing interval between the effective and the subsequent smaller dose, the number of subjects showing sensitisation increases.

5. Following sensitisation, even in normal subjects, the responses obtained to small doses of tuberculin may be of the " tuberculous " type. The reaction of those recently tested must consequently be interpreted with caution.

6. The influence of these changes on the relationship between the dose of tuberculin and the size of response is considered.

7. The possible mechanism and significance of these findings, and the light which they throw on the nature of the " tuberculous " response, are discussed.

I am again indebted to Captain Anton Tabone, R.A.M.C., Sgt. A. O. Pawelski, Sgt. K. Hargreaves, Cpl. A. Congrave and Cpl. N. F. Bayley, who at various times acted as " second observers."

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TABLE I

Group	*Type of reaction to 10 t.u.*	*Sensitisation Second interval **				*Activation*	
		2–3 days		*4–9 days*			
		+	−	+	−	+	−
Non-tuberculous	Normal	17	5	19	3	24	20
Tuberculous	Normal	5	18	16	8	14	33
	Tuberculous	4	17	9	16	10	36

* Interval between 10 t.u. and second 1 t.u. dose

TABLE II

Second interval in days	*Type*	*Size as percentage of 10 t.u. response*			
		First 1 t.u. Response		*Second 1 t.u. Response*	
		0–30	35–65	35–65	>65
2–3	N/N	11	6	15	2
	TB/N	0	5	4	1
	TB/TB	2	2	2	2
4–9	N/N	12	7	9	10
	TB/N	9	7	11	5
	TB/TB	3	6	8	1

N/N: non-tuberculous patients: normal responses.
TB/N: tuberculous patients: normal responses.
TB/TB: tuberculous patients: tuberculous responses.

TABLE III

Type of first response	*Type of second response*			
	Second interval 2–3 days		*Second interval 4–9 days*	
	normal	*tuberculous*	*normal*	*tuberculous*
N/N	8	9	12	8
N/TB	5	4	3	12
TB/TB	0	4	0	9

TABLE IV

	Size as percentage of 100 t.u. response											
	1 *t.u.*						10 *t.u.*					
	First			*Second*			*First*			*Second*		
	0–30	35–65	> 65	0–30	35–65	> 65	0–30	35–65	> 65	0–30	35–65	> 65
N	8	0	0	7	1	0	5	3	0	2	2	4
TB	15	2	0	15	2	0	9	5	3	11	3	3

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THE PROGRESS OF THORACIC SURGERY FOR PULMONARY TUBERCULOSIS

(LATE RESULTS AT PRESTON HALL HOSPITAL, 1949-53)*

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During the last few years we have witnessed revolutionary changes in the surgical treatment of pulmonary tuberculosis. The introduction of antibiotics and their use for prolonged periods, great advances in anæsthesia, better understanding of pulmonary physiology and increased experience in post-operative management, have encouraged surgeons to adopt a more aggressive attitude and to treat a wider range of patients than before. But the difference of opinion regarding preliminary medical treatment and the indications for surgery have widened. Acute, exudative disease responds well to bed rest and chemotherapy, but when the toxic symptoms disappear and sputum becomes negative it is difficult to find the right course to adopt. Within the last few years medical collapse measures and deforming and often unsafe surgery have given way to prolonged chemotherapy and pulmonary resection.

At Preston Hall Hospital, by 1955, the operation of plombage has been abandoned, the thoracoplasties have struggled for survival and the number of resections has increased from 33 in 1954 to 111.

Nearly twenty years ago the late Mr. L. O'Shaughnessy and Dr. J. H. Crawford stated that "... there are two requisites in the successful exploitation of the surgical treatment of pulmonary tuberculosis. There must be a low post-operative mortality and the patient should rightly expect cure rather than mere improvement."

The results of thoracic surgery which we have obtained show that the first requisite has been achieved; since 1949 no patient has died during the immediate post-operative period following the operations of plombage, segmental resection or lobectomy. The question still remains, can we by present methods achieve the second requirement, that of permanent cure?

The following is a review of the late results of cases operated on between 1949 and 1953. In that period 185 thoracoplasties (3 bilateral), 97 plombages (5 bilateral), 36 segmental resections, 84 lobectomies (1 bilateral) and 23 pneumonectomies were performed (Table I). Pneumonectomy results are not included, as this operation usually represented a life-saving measure for severe unilateral tuberculosis. Within the last eight years the small number of these operations—from 8 to 12 per annum—has not changed, but whereas there was

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TABLE I.—TYPE OF CASE AND PRE-OPERATIVE CONDITION

	Thoracoplasty	*Plombage*	*Segmental resection*	*Lobectomy*
Sex				
Male	132	67	22	49
Female	53	30	14	35
	185 (3 bilateral)	97 (5 bilateral)	36	84 (1 bilateral)
Age				
Less than 20	1	3	1	4
20–30	87	44	19	33
30–40	66	32	15	33
40–50	25	12	1	9
Over 50	6	6	—	5
	185	97	36	84
Sputum				
Positive	158	63	17	53
Negative	22	29	12	20
No record of ever positive	5	5	7	11
	185	97	36	84
X-ray Picture				
Cavity	164 (3 bilateral)	72 (5 bilateral)	22	62 (1 bilateral)
Doubtful	—	4	1	—
No cavity	24	26	8	10
Solid lesion	—	—	4	5
Atelectasis	—	—	1	8
	188 (3 bilateral)	102 (5 bilateral)	36	85 (1 bilateral)

a 17·4 per cent. post-operative mortality rate, only 1 out of 12 patients died in 1954-55 (8·3 per cent.).

Those selected for surgery were mainly between 20 and 40 years of age, and although 31 thoracoplasties and 18 plombages were performed on patients over 40, only 1 segmental resection and 14 lobectomies were employed. There was radiological evidence of cavitation in most cases, with positive sputum within six months of operation, and a large number of these patients had been treated by one of the then popular collapse measures of artificial pneumothorax, pneumoperitoneum or phrenic crush and were operated upon when these failed, but only when the toxic symptoms had subsided. In most cases the blood sedimentation rate did not exceed 30 mm./1 hour prior to operation.

Thoracoplasties and plombages were performed generally in cases with extensive or bilateral disease of long-standing, while those of resection had unilateral or lobar distribution and were dealt with much sooner after diagnosis. This was probably due to the earlier introduction of chemotherapy and limited involvement in resection cases.

Segmental resections were rarely performed, for fear of reactivation, and in cases where small scattered nodules were seen or felt during the operation more lung tissue was sacrificed than would be now. Dissecting across such areas was considered highly dangerous and lobectomy rather than segmentectomy was employed.

The problem of "satellites" and the question of the danger of their reactivation on over-expansion was confusing. Some surgeons believe that, as collapse leads to healing of the tuberculous process, so over-expansion may produce reactivation. This is certainly a logical conclusion, but has not yet been proved. In our material we had two groups of patients—those who had a pneumoperitoneum and phrenic crush or thoracoplasty subsequently performed in the presence of post-operative residual space and palpable nodules in the remaining lobe, and those in which this type of disease was ignored and their future left to chemotherapy.

Pre-operative measures consisted of chemotherapy, bronchoscopy, bronchography, respiratory function tests and physiotherapy.

Chemotherapy came into general use only recently and therefore cases of thoracoplasty and plombage had been treated with antibiotics in a somewhat irregular manner. Only 123 patients in the thoracoplasty group had received a short course of chemotherapy. It was more popular in cases of resection, but on 34 occasions no chemotherapy was given pre-operatively and many had only a few days' treatment, usually Streptomycin 1 G. with PAS 12-20 G. daily. Sensitivity tests were carried out as a routine and patients for resection were sensitive to at least two antibiotics prior to operation.

Bronchoscopy was performed prior to thoracoplasty and plombage when endobronchial involvement was suspected and regularly before resection, although there is no uniformity of opinion now as to the necessity for bronchoscopy in every case of resection.

Bronchography became popular in 1952 and has been used in the majority of cases of resection as an adjunct to tomography. It enabled an estimate to be made of all the segments involved and served as a final check on the negativity of sputum.

Respiratory function tests consisted of vital capacity and an exercise test. They were carried out regularly in cases doubtful from the respiratory point of view and comparatively few patients with vital capacity below 2,000 ml. were accepted for surgery. The age of patients admitted continues to move upwards, but recent investigations of the respiratory function of tuberculous patients of 50 show that it compares favourably with healthy persons of the same age, and in the view of some authors ". . . with careful management before and after surgery in regard to conservation of respiratory function, the age as such should not be accepted as a contraindication to resection" (Kallqvist, 1956).

Physiotherapy usually commenced a week prior to operation and continued for several weeks, with particular emphasis on the diaphragmatic movements and effective expectoration.

Anæsthesia presented no particular difficulties. Thoracoplasties and plombages were usually carried out under local infiltration; resections under general anæsthesia in a closed-circuit method, with pentothal, curare, nitrous

oxide and oxygen. After general anæsthesia every patient was bronchoscoped at the end of the operation.

Blood was given regularly. In cases of first stage thoracoplasty or plombage an average of 2 pints and in cases of resection 3 pints were usually transfused.

After the operation of plombage or resection underwater drainage was applied, and recently suction has been introduced in cases of resection. This appears to have improved our immediate results.

In general, preference was given to oxygen by mask, which provides continuous and higher concentration, although this method requires highly skilled and uninterrupted nursing.

Bed rest following thoracoplasty or plombage continued for three to six months, but in cases of resection a more active programme was adopted and patients were usually upgraded four to six hours within four post-operative months, depending upon the type of disease. Non-cavitary cases with negative sputum were upgraded much more quickly and were mobilised in a day or two after operation for about a week; then post-operative bed rest continued, but rest in a chair instead of in bed has also been used, with good medical and psychological results.

All patients who had undergone lobectomy, segmental resection or plombage left the hospital with sputum converted to negative. Usually three direct and three culture tests were carried out (Table II).

Most of the post-operative complications were dealt with successfully.

Pneumothorax or hæmopneumothorax occurred in 43 cases of thoracoplasty and in 18 cases of plombage, as the result of damaged pleura during operation.

TABLE II.—POST-OPERATIVE COMPLICATIONS

	Thoracoplasty	*Plombage*	*Segmental resection*	*Lobectomy*
POST-OPERATIVE COMPLICATIONS				
Pneumothorax	43	18	—	—
Atelectasis	23	3	4	11
Contralateral spread	9	—	1	1
Homolateral spread	—	1	—	—
Atelectasis and contralateral spread	4	1	—	—
Hæmorrhage	9	—	—	9
Hæmoptysis	1	—	—	—
Space infection (pyogenic)	5	1	—	2
Space infection (tuberculous)	1	1	—	—
Marked dyspnœa	9	—	—	—
Wound rupture	4	1	—	—
Displacement of plombage spheres	—	1	—	—
Bronchopleural fistula	—	—	6	1
Injury to 1st dorsal root	2	—	—	—
Air leak over 2/52	—	—	3	3
POST-OPERATIVE DEATHS				
Lung œdema	5	—	—	—
Heart failure	2	—	—	—
Hæmorrhage	1	—	—	—
Hæmoptysis	1	—	—	—

It may seem that this number is high, but divided between fifteen surgeons the average is not unusual.

Atelectasis in the pre-chemotherapy era, in cases of thoracoplasty for extensive disease or especially in the presence of paralysed diaphragm, was fairly common and was dealt with by either posture or bronchoscopy. Methods of post-operative management both in nursing and physiotherapy improve continuously, and chemotherapy is also playing an important part in reducing the amount of bronchial secretions. Within the last year all our atelectatic cases have responded to posture or other forms of physiotherapy and post-operative bronchoscopy was not required.

Hæmorrhage occurred in 9 cases following thoracoplasty and in 9 cases of lobectomy, but only 1 patient died—(following thoracoplasty), the subclavian artery being injured during the operation and a small aneurysm rupturing in the Semb space two weeks later. Hæmorrhage in cases of resection should not lead to death unless there has been faulty surgical technique or the symptoms of hæmorrhage have not been observed in time. There was a difference of opinion concerning cases of large clotted hæmothorax after resection; some surgeons evacuated them early, others left them intact. No marked difference in the final results have been observed.

Infection (pyogenic) of the space occurred on eight occasions, but all cases responded well to antibiotics or drainage. Tuberculous space infection following operation occurred once following thoracoplasty and plombage respectively and was also dealt with successfully by drainage.

In cases of thoracoplasty, other complications occurred such as dyspnœa—the most common—due mainly to paradoxical movement of the chest, then wound rupture, pleural effusion, brachial plexus injury, and spread of the disease. Wound rupture, spread of the disease and displacement of the spheres each occurred on one occasion following plombage.

Bronchopleural fistula following segmental resection occurred in 16 per cent., and following lobectomy in 1·19 per cent. of cases. Formerly it was due to imperfect technique and insufficient experience in dealing with the problem. On a few occasions the space was drained for a long time, on others aspirations with instillations of antibiotics were resorted to or thoracoplasty was employed.

At present bronchopleural fistula in the absence of infection is dealt with as soon as possible by thoracotomy and suture of the leaking bronchus, and by thoracoplasty in addition if the residual space remains.

Post-operative Mortality. In cases of plombage, segmental resection and lobectomy between 1949 and the present date there was no post-operative mortality within eleven weeks following operation. In the thoracoplasty group 9 cases died as a result of hæmorrhage (1), hæmoptysis (1), heart failure (2) and lung œdema (5).

By the time of publication of this paper over 350 lobectomies and segmental resections have been performed, with no mortality, although the range of age and extent of disease in cases selected for surgery has substantially increased.

Late death following thoracoplasty occurred in 2 cases after thoracoplasty, in two and three years respectively. One patient died of pneumonia, the the other as a result of pneumonectomy. In the case of plombage, late death occurred on two occasions after the cavity ruptured into the extraperiosteal

TABLE III.—FOLLOW-UP RESULTS

	Thoracoplasty	*Plombage*	*Segmental resection*	*Lobectomy*
Time since operation				
Less than 1 year	7	2	4	4
1–2 years	37	27	24	46
2–3 years	34	34	5	25
3–4 years	47	16	3	6
4–5 years	24	4	—	—
Over 5 years	25	12	—	—
Died	11	2	—	3
Present condition				
Good, working	137	72	31	74
Good, negative, not working	10 } 152 (82%)	2 } 85 (87·62%)	4 } 35 (97·22%)	4 } 78 (92·85%)
Satisfactory, sputum negative, convalescing	5	11	—	—
Awaiting surgery	—	1	—	—
Unsatisfactory, positive, not working	21 (11·35%)	3 } 6 (5·15%)	1 (2·77%)	3 (3·57%)
Unsatisfactory, sputum not examined, not working	—	2	—	—
Late death	2 (1·08%)	2 (2·06%)	—	2 (2·3%)
Lost sight of	1	3	—	—
Killed in accident	—	1	—	—
Suicide	—	—	—	1
Died post-operatively	9 (4·8%)	—	—	—
	185 (188)	97 (102)	36	84 (85)
Late deaths				
Pneumonia	1	—	—	—
Heart failure following pneumonectomy	1	—	—	—
Bronchopleural fistula (plombage infection)	—	1 related to operation	—	1 related to operation
Plombage infection (bronchopleural fistula)	—	1 related to operation	—	1 not related to operation
Suicide	—	—	—	1
Lost sight of	—	3	—	—

space, despite efforts to save the patients by lobectomy in one and thoracoplasty in the other case.

Late complications consisted of two tuberculous space infections following resection and ten following plombage.

Tuberculous space infection following plombage operation is a formidable complication in the presence of bronchopleural fistula after rupture of the tuberculous cavity. Infection without fistula is not dangerous and was dealt with by removal of plombage material and conversion to thoracoplasty. Those patients were usually in good condition, their disease was quiescent and the post-operative course following thoracoplasty was generally smooth and uneventful. In our series we employed lucite or polythene spheres and we have never had any difficulty in removing them.

Present Condition. There are now 350 patients in good or satisfactory general condition, grouped as under:

		Working
Thoracoplasty	152 (82·16%)	137
Plombage	85 (87·62%)	72
Lobectomy	78 (92·85%)	74
Segmental resection	35 (97·22%)	31
	350	314

In many cases patients who are working have not had their sputum examined recently. This applies in particular to those who have undergone resection and who are probably regarded by their chest physicians as finally "cured."

There still remain 21 patients in the thoracoplasty group with positive sputum, 3 in the plombage group, 1 in the segmental resection group and 3 in the lobectomy group.

There were 12 supplementary operations following thoracoplasty—(5 pneumonectomies, 5 lobectomies, 2 revision thoracoplasties) and 18 following plombage (1 pneumonectomy, 9 thoracoplasties with the removal of spheres, 8 lobectomies), 1 following lobectomy (thoracoplasty) and 8 following segmental resection (2 pneumonectomies, 3 thoracoplasties, 2 lobectomies and 1 segmental resection).

In cases of lobectomy and segmental resection, 65 patients have returned to their former occupation; in the plombage group the number is 34 and in the thoracoplasty group, 73. The remainder changed their occupations to something similar, or, in the majority of cases, to lighter work. Out of a total number of 402 patients only 3 were lost sight of (Table III).

Conclusion

Over 350 segmental resections and lobectomies were performed at Preston Hall Hospital between 1949 and the present date, and we have had no post-operative mortality.

In the valuation of results, although no final conclusions have been drawn as the picture of surgery in pulmonary tuberculosis is still changing and improves from year to year, in the light of our experience the operation of resection supported by chemotherapy—even accepting quite a high incidence of complications—seems the most effective and safe.

I should like to express my thanks to Dr. Temple Clive, Physician-Superintendent of Preston Hall Hospital, for his interest and valuable assistance in preparing this paper, and to Professor Heaf for his helpful criticism and final corrections.

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TUBERCULOUS CAVITY HEALING AND BRONCHOGRAPHY

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Pagel and Simmonds (1955) consider that the tuberculous cavity may heal in one of three ways:

1. By inspissation.
2. By fibrous scarring.
3. By "open cavity healing," in which the cavity wall is replaced by non-specific granulation tissue.

This form of healing used to be rare (Pinner, 1937). Medlar (1955) states that he has never seen a completely healed open tuberculous cavity. However, recently Denst and Russell (1956) have reported sterilisation of open cavities in 9 out of 57 resected specimens from patients treated with streptomycin and isoniazid.

Before the days of chemotherapy an important stage in the process of cavity healing was obliteration of the bronchus at the bronchocavitary junction. Several of the textbooks on tuberculosis mention that the tuberculous cavity, in contrast to the non-tuberculous bronchiectatic cavity, is not filled at bronchography owing to stenosis or obliteration of the draining bronchus, rather than to the type of radio-opaque material used. However, since chemotherapy was introduced, Auerbach and others (1953) have shown that in one stage of open cavity healing there is re-epithelialisation at the bronchocavitary junction.

Reviewing in this light 300 bronchograms performed in this hospital during the last two years, we found that radio-opaque material had entered tuberculous cavities in 19 cases. An aqueous suspension of propyliodone was the medium used in every case, and most of the bronchograms were done as a combined procedure with bronchography (Kalinowski and Lloyd, 1956).

At first we hoped that this might be a sign of complete open cavity healing, especially as all cases were sputum negative at the time of bronchography. However, although in all cases in which histological examination was undertaken there was some degree of healing of the cavity wall, tuberculous granulation tissue was still present in most. Nevertheless, although in our cases only partial healing was the rule, recent literature suggests that complete healing is becoming more common. As yet there is no way of distinguishing those cavities which will heal completely under the influence of prolonged chemotherapy, and only time will show whether patients with residual cavities can safely avoid surgical intervention.

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Illustrative Cases

1. D.H., aged 45. Pulmonary tuberculosis was diagnosed in October 1943, when a chest X-ray showed extensive disease in the right upper zone with a large apical cavity. Acid-fast bacilli were isolated from the sputum. Various combinations of streptomycin, sodium paraminosalycylic-acid (PAS) and isoniazid were administered over the next thirteen months, after which the chest X-ray showed a collapsed right upper lobe with the large cavity still present. Repeated examination of the sputum did not reveal the presence of tubercle bacilli. A right bronchogram showed marked crowding of the upper lobe bronchi, with some opaque medium present in the cavity. A right upper lobectomy was done.

The specimen: A rather shrunken right upper lobe covered by thickened pleura. There is a large trabeculated thin-walled cavity occupying the whole of the apex of the specimen surrounded by densely collapsed fibrotic lung, and without doubt this cavity communicated with at least one, if not more, bronchi.

Microscopy: The cavity lining consists partly of normal ciliated columnar epithelium, partly of epithelium undergoing squamous metaplasia, and partly of active tuberculous granulation tissue. In one Ziehl-Neelsen stained section no acid-fast bacilli were found.

2. J.S.H., aged 39. Pulmonary tuberculosis was diagnosed in January 1955, and he was admitted to hospital. Tubercle bacilli were found in his sputum. Chest X-ray showed a dense opacity in the right upper zone containing a cavity, with a considerable degree of collapse in the upper lobe. Chemotherapy was administered in the form of "Nupasal," an analogue of isoniazid, and PAS for eight months, followed by streptomycin and PAS over the next ten months. Tubercle bacilli could never be found in the sputum after April 1955. In October 1955 a right bronchogram showed the presence of propyliodone in the cavity (Fig. 1). A right upper lobectomy was carried out in November.

The specimen: The lobe contains a cavity 2 cm. in diameter, in direct communication with a large bronchus. The cavity lining is shiny and smooth, with a few ulcerated areas.

Histology: The cavity lining is naked collagen with areas of tuberculous granulation. No epithelial lining seen.

3. R.J.R., aged 24. Pulmonary tuberculosis was first diagnosed in January 1951, when the patient had a left pleural effusion. In August 1954 he developed a productive cough. When examined three months later tubercle bacilli were found in the sputum, and X-ray showed bilateral disease with a large cavity at the left apex. Various combinations of streptomycin, PAS and isoniazid were given for the next eighteen months. A chest X-ray then showed hard striate shadowing radiating upwards and outwards in the left upper zone, and a large apical cavity. Tubercle bacilli could no longer be isolated from the sputum. A left bronchogram showed opaque material in the left apical cavity (Fig. 2). Surgical treatment was not recommended.

4. G.B., aged 24. Pulmonary tuberculosis was diagnosed in 1949, and cavitation was present in the right upper lobe soon after diagnosis. During the next five years he was treated with pneumoperitoneum, phrenic crush, and large amounts of PAS, isoniazid and streptomycin. On admission to hospital in August 1955 the chest X-ray showed a cystic appearance in the right upper

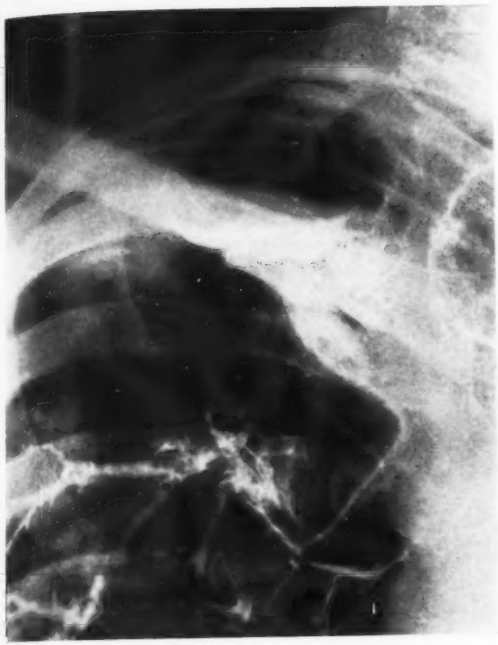

FIG. 1.—Right bronchogram showing cavity right upper zone with propyliodone in the cavity.

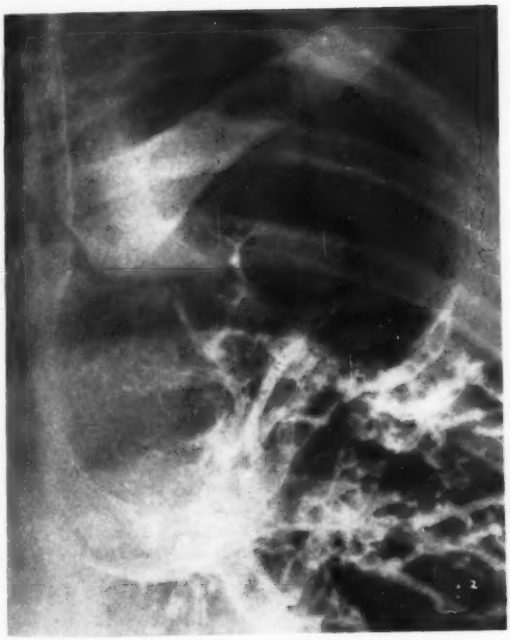

FIG. 2.—Left bronchogram showing opaque material in the left apical cavity.

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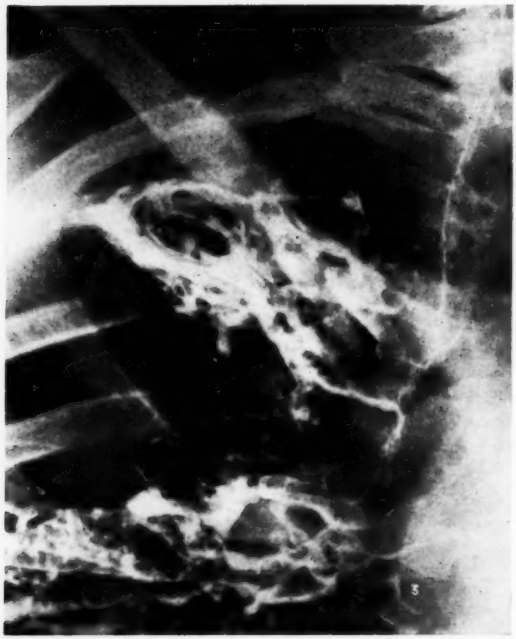

FIG. 3.—Right bronchogram showing gross cystic change in the right upper lobe.

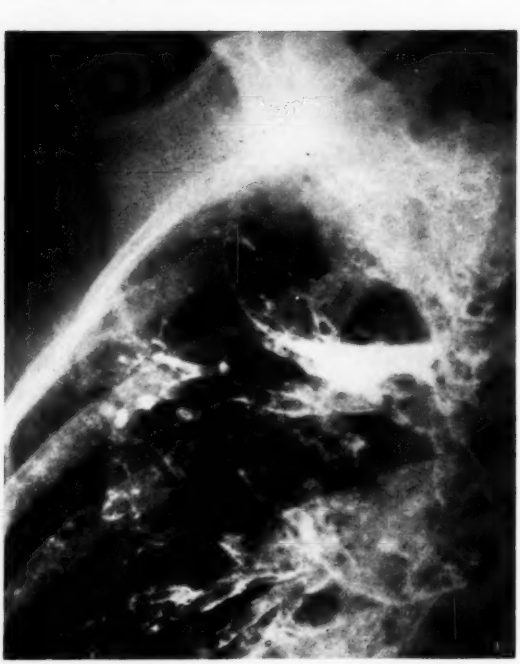

FIG. 4.—Right bronchogram showing some propyliodone entering the cavity in the right upper zone.

zone. No tubercle bacilli were found in the sputum. A right bronchogram showed gross cystic change in the right upper lobe (Fig. 3). In November the right upper lobe and apical segment of the right lower lobe were resected.

The specimen: Contains a large system of intercommunicating cysts without much evidence of tuberculosis.

Microscopy: Simple bronchiectasis with fibrosis of parenchyma. Apart from an occasional, partly calcified, small fibro-caseous focus there is no evidence of tuberculosis.

5. W.K., aged 33. Pulmonary tuberculosis was diagnosed in January 1955, when the chest X-ray showed infiltration and cavitation in the right upper lobe, and tubercle bacilli were found in the sputum. She was treated continuously by various combinations of isoniazid, streptomycin and PAS for the next fifteen months, after which the chest X-ray showed a cavity 5 cm. in diameter in the right upper zone, with some infiltration in the rest of the right upper lobe. A right bronchogram was done, and some propyliodone entered the cavity (Fig. 4). A right upper lobectomy was carried out.

The specimen: The posterior segment contains a cavity approximately 4 cm. $\times$ 3 cm. $\times$ 2·5 cm. in diameter.

Microscopy: The cavity is lined by loose collagen with a thin layer of tuberculous granulation tissue forming the free surface.

An analysis of our 19 cases shows that all had had anti-tuberculous chemotherapy for a minimum of six months, and all were sputum negative at the time of bronchography. The patency of the bronchi leading to the cavities outlined at bronchography suggests that epithelialisation had already commenced, at least at the bronchocavitary junction.

No definite clinical conclusions of practical importance can be drawn from these observations, but the following points emerge: (1) If cyst-like spaces are outlined at bronchography, tuberculosis must be considered in the differential diagnosis. (2) Some degree of healing of the draining bronchus must occur before the opaque material can enter the cavity.

In 19 of 300 bronchograms performed on patients with pulmonary tuberculosis a partly outlined cavity has been seen.

All the patients had had a fairly long period of chemotherapy. Tubercle bacilli had been isolated from the sputum of all cases at the onset of treatment, and could no longer be found at the time of bronchography. The patency of the bronchi leading to the outlined cavities may indicate that some degree of healing was taking place.

We wish to thank Dr. T. W. Lloyd for his interest and encouragement, and Dr. F. Kurrein for the pathological reports.

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PNEUMOPERITONEUM TREATMENT IN PULMONARY TUBERCULOSIS

A BRONCHOGRAPHIC STUDY

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Introduction

In the past ten years pneumoperitoneum has enjoyed great popularity in the treatment of pumonary tuberculosis. It has done so mainly at the expense of artificial pneumothorax. This has been due to several factors: (*a*) it is inducible in almost all instances; (*b*) it is comparatively easy to administer and control; (*c*) it is completely reversible; (*d*) there is very small risk of complications, especially the unexpandable lung; and (*e*) it can be easily restarted.

The efficiency of this treatment, with or without phrenic crush, is generally accepted. Moyer (1949) in a clinical and radiological assessment of 550 consecutive cases claimed cavity closure in 30 per cent. and sputum conversion in 79 per cent. of far advanced cases. Trimble *et al.* (1948) made a very comprehensive study of 407 consecutive cases treated by pneumoperitoneum supplemented by some form of phrenic paralysis in 78 of them. They concluded that an adequate pneumoperitoneum was valuable in that the period of complete bed rest was shortened and the sputum converted more quickly. Fraser (1950) reviewed 100 patients and had 33 per cent. successful results.

Some controversy, however, still exists over the sites of disease most amenable to pneumoperitineum treatment and also over its exact mode of action. As to site of lesion, in the two large series quoted above cavity closure seemed to occur equally in all areas of the lung.

Peter Edwards and Logan (1945) came to the conclusion that if the elevation of the diaphragm were adequate, the site of the cavity mattered less than the type of disease surrounding it—recent or fibrotic. Powell-David (1954) felt that pneumoperitoneum was most effective against lesions in the apical lower segment and in " the upper part of the lower lobe. " Fraser (1950), on the other hand, noticed better results (40 per cent.) in upper zone lesions. It is my impression that in most sanatoria and chest clinics it is taken as a working principle that pneumoperitoneum can influence lesions which appear in the X-rays below the level of the clavicle.

As regards the way in which pneumoperitoneum exerts its influence, several theories have been put forward. There seems to be general agreement that its most important function is to diminish the volume of the lung, thus encouraging relaxation of lung tissues and affording rest to the diseased part. Hiatt and Mitchell (1947) list the following factors: (*a*) Relaxation of elastic lung tissue promotes selective collapse in the more diseased part and, consequently, approximation of cavity walls. (*b*) Bronchial distortion and occlusion cause

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collapse of the diseased area, the air in the cavity is gradually absorbed and healing occurs. (*c*) Diminished blood circulation reduces the hazards of hæmatogenous spread and promotes fibrosis. (*d*) Lymph stasis also promotes fibrosis and may explain the diminution in constitutional symptoms following pneumoperitoneum induction. These last two factors are also mentioned by Pinner (1945) and by Calix and Jacobs (1948).

O'Connor (1947) is less enthusiastic about the value of pneumoperitoneum —at least in the presence of pleural adhesions. After discussing the physiology of respiration in the free and in the adherent pleura, he concludes that in the presence of extensive adhesions the lower zone is relaxed after induction of pneumoperitoneum but the middle and upper zones are not. He even goes further and states that when the lower zone is collapsed by the pneumoperitoneum there is a reflex hyperfunction in the upper part of the lung—the part which so often needs most rest. He reviews the effect of pneumoperitoneum treatment on nine cases who had an adherent pleura (this was presumed from the fact that attempts at inducing an artificial pneumothorax were unsuccessful). He showed that in such instances the raised diaphragm only caused a collapse of the adjacent lung tissue. The rest of the lung was not dimished in volume, as shown by a fixed lung marking on X-rays which did not alter its position before and after induction. All this does not accord with the commonly expressed opinion that pneumoperitoneum is indicated when pneumothorax is impossible because of adhesions.

Nevertheless O'Connor's conclusions appear to be quite logical. It was for this reason that this present study was undertaken. It was thought that by doing bronchograms on a number of patients who were undergoing pneumoperitoneum treatment some clearer idea could be obtained of the segments of lung which were genuinely relaxed by diaphragmatic elevation.

Selection of Cases

All bronchograms performed on patients in the past twelve months who had a pneumoperitoneum were examined, and if the rise of the diaphragm was satisfactory they were included in this study. The bronchograms were done either because bronchiectasis or collapse was suspected or in order to try to localise the disease prior to surgery. Six such bronchograms were included. It was also thought that it might be helpful for the purpose of this study to obtain bronchograms before and after pneumoperitoneum induction. In this way it was hoped that an even more precise idea would be obtained of which segments were most affected by elevation of the diaphragm. Nine of these were done. Unfortunately a good diaphragmatic elevation was obtained in only five, so that the other four were not included. These nine patients were not selected for any special reason. They had had consecutive pneumoperitoneum inductions, and had agreed to have two sets of bronchograms.

Bronchogram Technique and Complications

The cricothyroid method was used in all instances. This method was chosen not because it was thought to be superior to the others but because of greater experience and familiarity with it. One grain of phenobarbitone was given

three-quarters of an hour before transfer to the X-ray department and Xylocaine 2 per cent. was used as an anæsthetic. Oily Dionosil (60 per cent.) was the contrast medium used, from 12 to 15 ml. being introduced, depending on the size of the chest. X-rays were then taken in the postero-anterior and lateral positions. In those patients who had both pre-induction and post-induction bronchograms great attention was paid to positioning during X-rays. On returning to the wards the patients were instructed to get rid of the Dionosil by postural drainage.

No serious complications were met with. A slight rise of temperature up to 99·2° F. was observed in some patients, but this lasted only for twenty-four to forty-eight hours. No exacerbation or spread of tuberculous diseases occurred.

Results

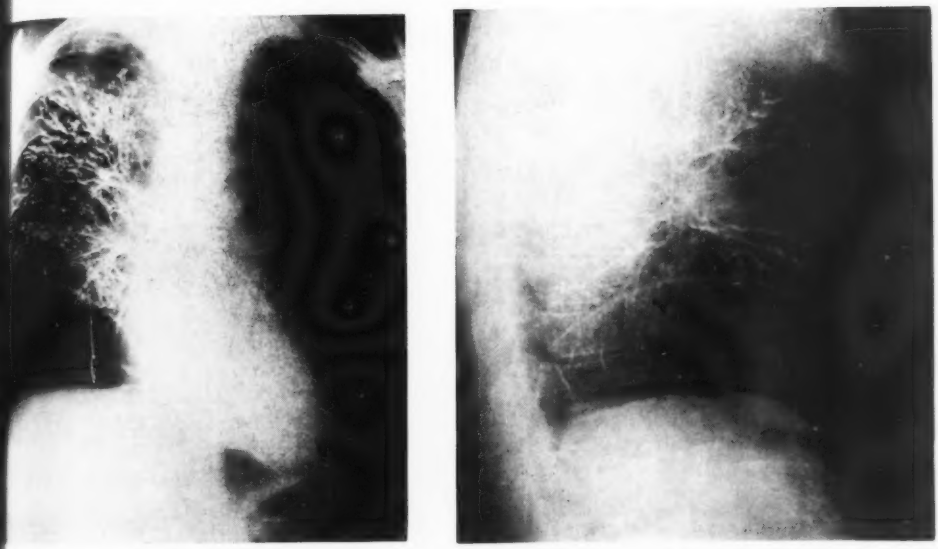
Six post-induction bronchograms were examined. The average diaphragmatic elevation was 3¼ inches. Except for minor variations the pattern of collapse was remarkably similar in all. The lower part of the bronchial tree was very considerably distorted but the upper part was of normal structure. Closer examination showed that the brunt of the collapse was borne by the basal segments of the lower lobe. In all bronchograms these seemed to be squashed together, the bronchi were distorted, twisted and pushed backwards and largely inwards towards the mediastinum. The middle lobe (or lingula if on the left side) was also collapsed to some extent, though distortion of the main middle lobe bronchus was seldom seen. The upper lobe and the apical segment of the lower lobe were the least affected. (See Fig. 1*a* and *b*.)

These findings were confirmed by the sets of bronchograms done before and after pneumoperitoneum induction. Tracings were done of all these ten sets of bronchograms and the corresponding ones were then superimposed. This gave a very clear idea of where collapse had occurred in each case and to what extent. Only in one instance was there a " concentric shrinkage " of the whole bronchial tree. In this all the segments of the lung seemed to become remarkably smaller because of the rise of the diaphragm, but even here the upper lobe was not as collapsed as the rest of the lung. In the other four sets of tracings the upper lobe and the apical lower bronchi could be superimposed perfectly on top of each other; there was hardly any difference in size, shape or form before or after induction of pneumoperitoneum as far as their segmental and subsegmental bronchi were concerned. (See Fig. 2*a*, *b*, *c*, *d*.) Two of these patients later came to surgery and on opening the chest it was found that in one the pleura was completely free and in the other there were only a couple of very thin adhesions over the upper lobe.

Discussion

Banyai (1946) in his comprehensive researches into the effects of pneumoperitoneum treatment concluded that elevation of the diaphragm produced a reduction in lung volume and that this reduction was distributed fairly evenly through the whole area of the lung. Bronchograms done on patients undergoing pneumoperitoneum treatment would seem to disprove this theory. It seems that the diminution in lung volume is mainly at the expense of the basal seg-

PLATE XI



4, 1 (*a* and *b*).—Postero-anterior and lateral views of right bronchograms showing crowding of bronchi of the middle lobe and of the basal segments.

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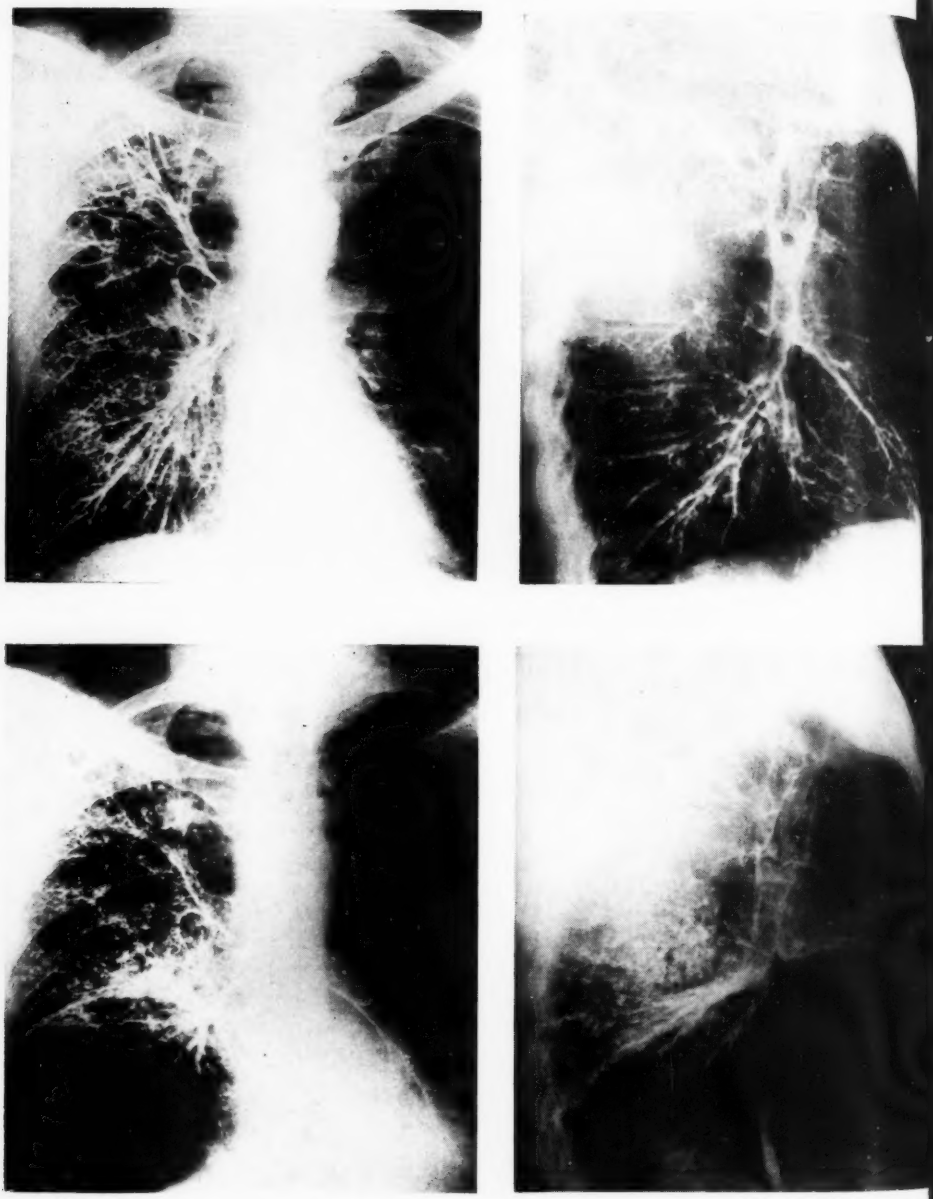

FIG. 2 (*a*, *b*, *c* and *d*).—Bronchograms done on a patient before and after pneumoperitoneum induction. Po
anterior and lateral views.

ments of the lower lobe and the lower part of the middle lobe. This localised collapse was thought by O'Connor to be due to pleural adhesions. Two of our patients were found at operation to be free of adhesions, so that this alone cannot be the cause of non-collapse of the upper zones. Clifford Jones and McDonald (1943) compared the relaxation obtained in the lung after pneumoperitoneum to " a sponge pressed against a flat surface by the palm of the hand, thus producing compression of the sponge tissue at either end but relatively little in the middle portion." Our bronchograms seems to show that in most cases " the sponge " is compressed to any worth-while extent only at the point of pressure—*i.e.*, the diaphragm as it rises compresses only the contiguous tissue, the rest of the lung remaining unaffected.

Summary

1. A brief review of the literature dealing with the mode of function of pneumoperitoneum treatment in pulmonary tuberculosis is given.

2. Bronchograms were done on six patients undergoing pneumoperitoneum treatment and on five patients before and after induction of their pneumoperitoneum.

3. These bronchograms showed that very rarely were the upper lobe and the apical segment of the lower lobe affected materially by elevation of the diaphragm.

I would like to thank Dr. J. Houston and Dr. Robert Coope for their encouragement and advice.

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CORTISONE-ANTIMICROBIAL THERAPY IN TUBERCULOSIS

By Lucien H. Harris*

From the Whittington Hospital, London

The suppression of granulation tissue formation and fibroblastic repair by cortisone or by corticotrophin suggested a new therapeutic régime for tuberculosis—*i.e.*, the concurrent administration of one of these steroids with the usual antimicrobial drugs. This paper records the effects of cortisone-antimicrobial therapy in 14 cases and a review of the literature.

Case Reports

The clinical details of the 14 cases are summarised in Table I. In 10 patients the effects of adding cortisone to their régime were dramatic. In twenty-four to forty-eight hours they felt well: some were frankly euphoric. Their appetites increased enormously and their pyrexia subsided. In some there was notable relief of cough, in others the E.S.R. fell rapidly. A gain in weight of 7 to 28 lb. occurred in 8 cases. In several these symptomatic effects persisted after discontinuing cortisone. There were no radiological changes except in Case 5 discussed below.

Discussion

There is very little evidence that cortisone or corticotrophin exerts any effect on tuberculous lesions treated with adequate antimicrobial drugs.

Apparently Adverse Effects. Meyer *et al.* (1952) reported 3 cases of advanced pulmonary tuberculosis treated with corticotrophin and antimicrobials. One was temporarily improved clinically, one showed no change and the third deteriorated progressively. This is likely to occur in such cases regardless of steroid therapy. Bulkeley (1953) had four deaths in a series of 31 cases of tuberculous meningitis treated with corticotrophin and antimicrobials. These patients all had advanced disseminated disease when first seen and received the steroids for one week only. Ashby and Grant (1955) recorded the breaking down of lymph glands in one of their cases while on cortisone-antimicrobial therapy. In one patient (Case 8) a new gland appeared during combined therapy; in another (Case 6) a cervical gland disappeared during treatment. It is unreasonable to attribute both resolution and exacerbation to the cortisone. Kendig *et al.* (1956) described the increase in size of a non-tuberculous cyst during combined therapy for tuberculous meningitis. A similar event occurred in one patient in this series (Case 5). The probable explanation is that prolonged recumbency altered bronchial mechanics so that these upper lobe cysts were converted into tension cavities. Smith *et al.* (1956) mention 2 cases of tuberculous meningitis who died in spite of treatment with cortisone

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TABLE I

Patient	Sex	Age	Type of disease	Dosage of cortisone mgm./day	Antimicrobial therapy	Weeks of combined therapy	Effects
1	F	24	Acute bronchogenic unilat. cavit. Poor response to antimicrobials	50–100	S1H300P16	6	Afebrile in 24 hr. E.S.R.88→11. Wt.+21 lb. Sputum converted. X-ray unchanged.
2	F	28	Acute lobar consolidation. Poor response to antimicrobials	50–75	S1P16	4	Afebrile in 48 hr. Wt.+7 lb. Sputum converted. X-ray unchanged.
3	F	37	Acute bronchogenic bilat. cavit. Poor response to antimicrobials	50–150	S1H200→ P16H200	9	Afebrile in 24 hr. X-ray unchanged. Vestibulotoxicity of strep. unrelieved by cortisone.
4	M	66	Acute bilat. bronchogen. Unilat. cav. Poor response to antimicrobials	100	S1H200→ P12H200	12	Afebrile in 24 hr. E.S.R. 30→10. Wt.+11 lb. X-ray unchanged. Ocular effects of strep. unrelieved by cortisone.
5	M	39	Tuberc. meningitis. Chronic fibrocaseous pulm tuberc. Poor response to antimicrobials	100–200	S1H500P16	9	Temporary clinical improvement. X-ray showed enlargement of "cavity." *Necropsy:* fibrogran. tubercles L.L.L., non-Tb cysts upper lobes, healed T.B.M.
6	F	27	Cervical, paratracheal and hilar adenitis. Poor response to antimicrobials	150	S1H200P12	9	Afebrile in few days. R. supraclavicular gland disappeared. E.S.R. 58→3. Wt.+20 lb. Gastric lavage converted. X-ray unchanged.
7	F	16	Healed miliary lungs. Relapse of tuberc. mening. with oculomotor palsies and papilloedema	50–150	S1H400P16	20	Headache and vision improved in 24 hr. Wt.+28 lb. Ocular palsies improved. Papilloedema→partial optic atrophy. C.S.F. converted. X-ray unchanged.
8	F	75	Cervical, paratracheal and hilar adenitis. Tuberc. prepatellar bursitis and palmar ganglion. Hypersensitive to streptomycin	75	P12H200	3	Exfoliative dermatitis rapidly cleared. New gland appeared (L. cervical) required aspiration. X-ray unchanged.
9	F	28	Relapse under thoracoplasty. Hypersensitive to strep. and PAS.	75	P16H200	3	Satis. desensitisation. Wt.+9 lb. X-ray unchanged.
10	M	32	Chronic bilat. fibrocaseous. Hypersensitive to strep. and PAS.	50–150	S1H200	6	Satis. desens. Wt.+14 lb. X-ray unchanged.
11	F	17	Pleural effusion with apical infiltration. Hypersensitive to streptomycin	75–200	P12H200	3	Exfoliative dermatitis rapidly cleared. X-ray unchanged.
12	F	54	Chr. unilat. fibrotic. Amyloidosis. Hypopituitarism	15	H500N500	39	Mental state improved. Sputum converted. X-ray unchanged.
13	M	61	Chr. unilat. cav. Addison's disease	25	S1P16	36	Metabolism restored. Sputum converted. X-ray unchanged.
14	M	45	Chr. bilat. fibrocaseous. Unilat. cav. Rheumatoid disease	15–30	P16H200	13	Relief of arthritis. X-ray unchanged.

S1 = Streptomycin 1 g. daily
H200, 300, 400, 500 = Isoniazid 200, 300, 400 or 500 mg. daily
P12, 16 = P.A.S. 12 or 16 g. daily
N500 = "Nupasal" 500 mg. daily

and antimicrobials. One of these had Addison's disease and the other had glandular fever and exfoliative dermatitis as complications.

Apparently Beneficial Effects. In 27 of his 31 cases of tuberculous meningitis treated with corticotrophin-antimicrobial therapy, Bulkeley (1953) obtained good results. This was probably due to the use of isoniazid, since corticotrophin was used only during the first week of treatment in the majority of his cases. Isoniazid had only just been introduced at the start of his series and it is known that the results of treatment of this condition are now superior to those of the pre-isoniazid era (Lorber, 1956).

Ashby and Grant (1955) treated 6 cases of tuberculous meningitis with cortisone and antimicrobials; all recovered, but one developed spinal block after discontinuation of steroid therapy. The same criticism applies to these cases as to Bulkeley's series. The relief of cerebrospinal fluid block by cortisone or corticotrophin was reported in 2 cases by Kinsell (1952) and in 1 case by Shane *et al.* (1952). There is no proof that this was due to the steroid, since astonishing recoveries can occur without the use of cortisone or corticotrophin (Lorber, 1956). The temporary clinical remission of tuberculous meningitis noted by Johnson (1955) was only symptomatic. Similarly, in one of my patients (Case 7) recovery might have occurred without cortisone.

Smith *et al.* (1956) described dramatic clinical results in 3 cases of tuberculous meningitis treated with cortisone and antimicrobials, but all three later developed classical tuberculous meningitis. A fourth patient recovered from a severe reaction to P.P.D. as a result of cortisone therapy.

Sors *et al.* (1954) and Lebacq and Tirzamalis (1954) considered that some pleural and pericardial tuberculous effusions cleared more rapidly with combined therapy. Their criterion was that in 17 out of 31 cases there was clearing of fluid in three to six weeks. Similar results may, however, be obtained without the use of steroids.

In 4 of the 5 cases of Addison's disease with pulmonary tuberculosis treated with cortisone and antimicrobials by Browne *et al.* (1954) there was improvement in the pulmonary lesions. Three of these cases had received no previous antimicrobial therapy and the fourth had only received a short course of PAS in the past. The result in these patients was almost certainly due to the antimicrobial therapy.

Houghton (1954) noted radiological improvement in some patients with exudative pulmonary lesions on combined therapy. These are, however, the very cases that improve most on antimicrobials alone and it is significant that Houghton himself attributed the major benefit to them. He also had several patients whose lesions were unchanged by corticotrophin-antimicrobial therapy. Slight radiological improvement occurred in a patient with disseminated lupus erythematosus and pulmonary tuberculosis on combined therapy (Johnson and Davey, 1955). This patient had never before received antimicrobial therapy, so there is no evidence that the steroid caused the improvement. There was no radiological change in either of the 2 cases of pulmonary tuberculosis treated with cortisone-antimicrobial therapy by Gros and Tilling (1955). Cochran (1954) recorded radiological improvement in 4 out of 9 cases of pulmonary tuberculosis treated with cortisone and antimicrobials. There was no evidence that these cases would not have responded equally without cortisone. Later Cochran *et al.* (1956) described "accelerated" improvement in some

cases treated with combined therapy. This, of course, is only a clinical impression and the cases said to have shown significant improvement had, as in Houghton's series, acute exudative lesions. Climie *et al.* (1956) reported 3 cases of pulmonary tuberculosis with rheumatoid disease in which corticotrophin appeared to have caused improvement in the pulmonary lesions. In these patients corticotrophin was added to their treatment after only a short period of antimicrobial therapy and it is possible that improvement would have occurred without it.

Conclusions

From this review of the literature there is no definite evidence that cortisone or corticotrophin exerts any effect on the course of tuberculous lesions when given together with effective antimicrobial therapy. The absence of radiological changes in 14 cases supports this conclusion.

Dramatic clinical effects are often obtained. Cortisone may occasionally be indicated in patients with grave toxæmia to tide them over a difficult period. A prolonged study would be required to assess whether the ultimate prognosis was affected.

The value of cortisone in the management of hypersensitivity to antimicrobials is confirmed. Equally gratifying results have been obtained with antihistamine drugs in other patients, and it is suggested that steroids be reserved for very severe reactions or for cases not responding to simpler measures.

This series also confirms the safety of administering cortisone to patients with active tuberculosis, provided that adequate antimicrobial cover is given simultaneously.

Summary

The literature concerning the use of cortisone or corticotrophin with antimicrobials in the treatment of tuberculosis has been reviewed.

The safety of this régime, its dramatic symptomatic effects and the value of cortisone in suppressing hypersensitivity are confirmed.

It is concluded that cortisone has no effect on tuberculous lesions *per se* in patients treated concurrently with effective antimicrobial therapy.

I wish to thank Dr. G. A. Back for permission to report Cases 1 to 12 and Dr. Wallace Craig for permission to report Cases 13 and 14.

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REVIEWS OF BOOKS

The Practice of Medicine. Ed. by JOHN S. RICHARDSON. London: J. and A. Churchill Ltd. 1956. Pp. viii+1,076. Illus. 40s.

To encompass the ever-increasing medical syllabus of today in a single readable volume of 1,000 pages and in sufficient detail to enable the student to pass his final examinations is a commendable feat. This new book achieves it by concentrating on the essentials and avoiding the vague theory and speculation so commonly copied from textbook to textbook. There are fourteen contributors, half of them from St. Thomas's Hospital, and their variety of style adds to the readability of the text which is otherwise relieved by comparatively few illustrations. It is an orthodox textbook for students and practitioners with emphasis on the practical management of patients; an appendix covers the collection of specimens, normal values and diets, and guidance to further reading concludes most chapters.

The introductory chapter is a skilful précis of medical history, tracing for the student the development of modern concepts of the nature of disease, and an excellent chapter on antibacterial drugs precedes the detailed consideration of individual diseases. The relative space allotted to the different systems differs somewhat from other books. Diseases of the skin are deliberately omitted but a dermatologist contributes chapters on allergy, sarcoidosis and the collagen diseases. Psychiatry and neurology together occupy 300 of the 1,000 pages and share them equally. This generous allocation is in sharp contrast to the scant 30 pages devoted to the whole of the alimentary system; although commendable for its brevity this section is too condensed for a student's first text book. Sections on hæmatology, tropical diseases and endocrinology are concise and up to date. Chapters on the cardiovascular system occupy 86 pages and are easy to read and thorough; emphasis is on the clinical appraisal of the patient but adequate description of the modern diagnostic methods is included; minor criticism may be levelled where expressions of opinion are stated as facts, *e.g.* that " subcutaneous mercurial diuretics have largely superseded intramuscular injections of Mersalyl, etc."

Two authors contribute the respiratory disease section (153 pages) which, in keeping with modern thought, is prefaced by the essentials of respiratory physiology. Clinical description of disease entities is vivid and, in addition, the wide social aspect of the common chest complaints is constantly driven home. Respiratory tuberculosis and occupational lung disease are particularly well covered. Perhaps the student might expect to find pleurisy and pleural effusion dealt with in separate chapters and not only under the heading of tuberculosis, although the necessary information is there for him if sought; also some mention might have been made of hæmothorax and its management.

In general the teaching throughout is clear and sufficiently dogmatic to appeal to the student and busy practitioner. The standard of printing is good with few errors and the publishers deserve credit for producing a book of this calibre at such a reasonable price.

F. H. SCADDING.

Cancer of the Lung. By MILTON B. ROSENBLATT and JAMES R. LISA. London: Cumberlege, Oxford University Press. 1956. Pp. xiii+330. Illus. 120s. net.

In this volume an attempt is made to cover every aspect of cancer of the lung in 300 pages. A vast number of references are included and statistical

aspects are stressed at every stage. This means that the book reads rather like an encyclopædia and the personal opinions of the various authors are difficult to discover. On the other hand, there is probably no other volume upon this subject which contains such a mass of facts in so small a space. The opinions of others are adequately recorded and the world literature has obviously been studied in detail. The sections on pathology and cytology are particularly good. The reproductions of radiographs, which are of only moderate quality, might be considerably reduced in number in another edition.

This volume sets out clearly the vast amount of information which has accumulated on carcinoma of the bronchus and forms a valuable addition to the literature of the subject.

NEVILLE OSWALD.

Diagnosis and Treatment of Vascular Disorders (Angiology). Edited by SAUL S. SAMUELS, with 17 contributors. London: Baillière, Tindall and Cox Ltd. Pp. x+622. Illus. 128s.

The general surgeons' provinces are being steadily encroached upon as each new speciality emerges. Vascular disorders are a comparatively small subject, and yet it is considered that diseases of the blood vessels alone are sufficient to constitute a life-long study for a young physician or surgeon, and, as in the other specialities which have advanced so much in recent years, a team of workers is thought to be necessary.

Such a view is reflected in this book, to which there are seventeen contributors, three of whom hail from this country, from the University of Manchester. The authors include surgeons, physicians, and a physio-therapist. The book opens with a description of the anatomy and physiology of the blood vessels, and this is followed by an interesting account of the clinical examination of the patient, in which the special methods of investigation are described.

The field of vascular diseases is well covered, special chapters being devoted to angiography, local cold injuries, aneurysms, and, what is of more interest to physicians, Raynaud's disease, arteriosclerosis and atherosclerosis in diabetes, endarteritis obliterans, thrombo-angiitis obliterans, the scalenus anticus syndrome, polyarteritis nodosa and chronic œdema of the legs.

It comes as rather a shock to the reader in this country to find his old friend erythromelalgia described as " erythermelalgia."

From the patient's point of view angiography cannot be described as a pleasant performance, nor one devoid of risk, and it is gratifying to find that one of the surgical contributors has this in mind when he writes: " Angiography has potential dangers in the most experienced hands, and its indiscriminate use merely to obtain an interesting record is unwarranted."

The book is well produced, profusely and beautifully illustrated, and no physician or general practitioner could fail to benefit from reading it and keeping it as a book of reference.

G. E. BEAUMONT.

Principles of Chest X-ray Diagnosis. By GEORGE SIMON. London: Butterworth and Co. (Publishers) Ltd. 1956. Pp. x+183. Illus. 50s. net.

As the title of this book implies, it deals primarily with the principles of chest X-ray diagnosis, and this the author has achieved in a somewhat stimulating and unusual manner. Dr. Simon deals with X-ray shadows in a descriptive way, and arranges the chapters of the book around the radiographic appearances, rather than under pathological classifications. With this method, which is after all the practical way in which radiographs are approached, his

wide experience in chest radiology is put to full use and a logical deduction and correlation of shadows with pathological findings is achieved.

It may well be that his method of presentation will be adopted by others and will form a useful alternative to the more orthodox and uninspired. In addition to radiographic studies of the normal and pathological shadows in the chest, there are most helpful short chapters on radiographic techniques and dark-room methods.

This valuable book will no doubt be used as a basis of radiographic interpretation of chest disease by both clinicians and radiologists. The excellent and well-chosen illustrations go a long way to elucidate the factual description in the text.

R. E. STEINER.

Airborne Contagion and Air Hygiene. By WILLIAM FIRTH WELLS. Harvard University Press. 1955. Pp. 29+421. Illus. 48s. net.

This book, the fruits of many years of research, is written in part for laymen who wish to learn about air hygiene and in part for specialists. The first twelve chapters deal with the physics, aerodynamics, biology, biochemistry, physiology and parasitology of droplets and droplet nuclei, under the general heading of Airborne Contagion. The second half of the book relates to sanitary ventilation and air hygiene, with concluding essays on dust-borne infections and the ecology of droplet infections. There are also a summary, two appendices, a bibliography extending over twenty-five pages and an index of eighteen pages.

It will be evident that this is no ordinary work. In the detailed account of the investigations into airborne infection due credit is given to British workers, including some almost forgotten in their own country. How many people now remember the work of C. J. Thomas on measles in the Woolwich District in 1905? As a historical record the book is valuable, but it is more difficult to assess the full weight of its contribution to recent advances. The wording is sometimes so involved that the meaning is obscured, and as it is written for both laymen and experts there is considerable repetition.

The experimental work on which the book is based was carried out in America, and the sections dealing with field studies are more concerned with acute than chronic airborne infections, and especially with the results of attempts to control the spread of those diseases in schools by irradiation with ultra-violet light.

The earnestness and sincerity of the author, and the tremendous amount of research work undertaken, are most impressive, but in the end there is a sense of disappointment that, somehow or other, an important message has failed to come through.

A. LESLIE BANKS.

Diseases of the Heart and Circulation. 2nd Edition. Revised and enlarged by PAUL WOOD. London: Eyre and Spottiswoode (Publishers) Ltd. 1956. Pp. xxxviii+1,005. Illus. 5 gns. net.

The first edition of this book was reviewed in this Journal in April 1951. The second edition has been completely revised, in keeping with the advances in cardiology during the last five years, and the interpretation of symptoms and signs has been revised in the light of recent discoveries. The surgery of the heart, congenital heart disease, pericardial effusion and Pick's disease, ischæmic heart disease, the medical treatment of hypertension, are among the subjects which have been revised and adapted, and the author's views on pul-

monary hypertension have been admirably expressed in a new chapter on this subject.

In the main, the numerous illustrations are good, although a few are below standard, and it is unfortunate that a uniform system of either negative or positive prints for chest X-rays is not used. This minor criticism in no way detracts from this authoritative, up-to-date work, by one whose original contributions to cardiology, in the clinical and experimental fields, are recognised as outstanding.

The book can be thoroughly recommended to cardiologists, and to all who are interested in the wider aspects of thoracic medicine. These include the general physician and, no less, the chest physician.

Interesting Cases and Pathological Considerations. By F. PARKES WEBER. London: H. K. Lewis and Co. Ltd. 1956. Pp. iv+77. Illus.

Dr. Frederick Parkes Weber's new little book on " Interesting Cases and Pathological Considerations " is yet a further example of his incredible contributions to the literature on rare diseases.

In his ninety-fourth year, with his mind fully alert and active, he continues to advance the work on this subject, and in a chapter on some lesser-known diseases affecting the lungs he instances Sjögren's Disease, Oil and Lipoid Pneumonias, Nieman-Pick's Disease, Actinomycosis of the Lungs, Sclerodermia and the so-called Collagen Diseases. In this latter group of diseases he instances cases of rheumatoid nodules involving the lungs and pleura.

Reference is made to recent work on Honeycomb Lung, Malignant Leiomyomatous Infiltrations of the Lungs, and Pulmonary Tuberous Sclerosis. Reference is also made to Honeycomb Lung in relation to Eosinophilic Granuloma, Diabetes Insipidus, etc. In addition to these observations he is up-to-date with a reference to the Hamman-Rich Syndrome, Diffuse Interstitial Pulmonary Fibrosis. Dr. Parkes Weber is to be congratulated on his remarkable achievement.

Bronchologie. Technique Endoscopique et Pathologie Trachéo-Bronchique. 2 volumes. By ANDRÉ SOULAS and PIERRE MOUNIER-KUHN. France: Masson et Cie. 1956. Pp. 1,146 (2 volume total). Illus. 14,000 fr.

This second edition in two volumes, by André Soulas and Pierre Mounier-Kuhn, with an introduction by Chevalier Jackson and a foreword by Professor Robert Monod, is a comprehensive study of almost every aspect of tracheobronchial disease included under the general term " bronchology." It has now been entirely rewritten, and has twice the number of pages of the earlier edition, with 486 illustrations and 67 colour plates, as against the 304 illustrations and 24 colour plates of its original.

The anatomy and physiology of the bronchi and broncho-pulmonary segments, broncho-spirometry, the radiology of the chest including bronchography, tomography, tomo-bronchography, and a new feature described as cine-photography, all receive their due attention, with strikingly good illustrations. Bronchoscopy, its technique, its value in diseases of the trachea, all forms of bronchial disease including bronchitis, asthma, broncho-pulmonary suppuration, tuberculosis, benign and malignant tumours of the bronchi, are among the many subjects surveyed and discussed. This study is of particular interest to physicians and surgeons whose special activities lie in the sphere of diseases of the chest, but it is also of interest to the nose and throat surgeon,

the anæsthetist, as well as the general physician, the cardiologist and the pediatrician.

While the book is admirably produced and illustrated, references to British work are scanty, and it is irritating to find in a work of this nature a bibliography so slipshod in its compilation. In some cases the initials of the author are given, in others omitted, and in others incorrect. In some places the bibliography gives the authors' names in convenient alphabetical order, at other times the reverse. These minor points apart, the book can be most highly recommended.

PHILIP ELLMAN.

Cœur et Poumons. By. P. SOULIE and E. BRIAL, J. CARLOTTI, J. DI MATTEO, FR. JOLY, P. LAURENS, A. PITON, J.-R. SICOT, J. DELARUE, G. BROUET, R. DEPIERRE, M. BARIÉTY and J. PAILLAS. France Masson et Cie. 1956. Pp. 224. Illus. 1,600 fr.

The Medical Faculty of Paris began in 1947 a series of post-graduate refresher courses designed for doctors and specialists who wish to keep up to date with recent advances in medicine. With the new series which was introduced last year a different method of presentation has been adopted, and various experts in different fields have been invited to discuss a given subject from the point of view of the physician, surgeon, biologist, radiologist or specialist in some other appropriate branch.

The present volume contains three of these symposia. The first is concerned with the function of the heart. The chief subjects discussed are cardiac radiology, angio-cardiography and cardiac catheterisation, and each of these papers presented in this volume is a fair report upon the recent advances in these fields. Perhaps the reader is left with the impression that the clinical examination of the heart is becoming of less importance than the highly specialised investigations, although this conclusion was probably far from being the intention of the writers and editors.

The second section is devoted to the problem of diseases of the mediastinal glands, and the differential diagnosis of mediastinal tumours in general. The detection of glandular lesions in the chest depends to a large extent upon the interpretation of X-ray films, and it is disappointing to find so few illustrations provided in this section. There is not even a single picture of sarcoidosis nor a mediastinal tumour. One of the great problems of X-ray diagnosis in chest diseases is the distinction between enlarged hilar glands and prominent blood vessels, and a few illustrations would not have been amiss to assist the reader in making this distinction.

The final section deals with bronchial carcinoma and it is written by Bariéty and Paillas, who appear to remain unconvinced that cigarette smoking is a sufficient explanation of the great increase in the evidence of this disease. The section on treatment is extremely brief and the surgical results indicate a three-year survival period of 15 per cent. of the cases treated by resection. This figure seems to be depressingly low.

Les Fondements Anatomo-Radiologiques de l'Investigation Pulmonaire. By F. KOVATS JUN. and Z. ZSEBOK. France: Masson et Cie. 1955. Pp. 336. Illus. 8,000 fr.

This elaborate volume was first published at the end of 1953, and a second edition was presented a few months later, both being written in German. The third edition, revised and brought up to date, has been translated into

excellent French by E. Juhasz. Doctors Kovats and Zsebok have produced a comprehensive textbook on the Radiological Anatomy of the chest, and they give a clear explanation of recent advances in radiological technique and in the anatomical interpretation of X-ray films. The book is outstanding in presentation of its subject matter, which is matched by illustrations of equal merit.

The authors take care to point out that the X-ray examination of the chest, both by fluoroscopy and by films, is only one part of the clinical examination, and they emphasise the need for close co-operation between the radiologist and the clinician. Their book is presented as an exposition of the normal structure of the thorax and its contents, and they point out rightly that a clear understanding of the normal is essential to the correct interpretation of abnormalities in X-ray films.

In a book of this sort at least as much of the value rests upon the illustrations as upon the text, and no fault can be found with either aspect. It is a pity that there is as yet no internationally agreed nomenclature for the segments of the lungs, and a good deal of space is given to a consideration of the many systems advocated in the past twenty years; the authors have reached the compromise based on the International scheme, with modifications which follow the suggestions made by Kassay in 1950.

This is hardly a book for a general physician, but it should prove to be of very great value to those who are concerned with the interpretation of chest X-ray films.

Nouvelle Orientation du Traitement du Mal de Pott de l'Adulte. By S. DE SÈZE and J. DEBEYREI. France: Masson et Cie. 1956. Pp. 102. Illus. 900 fr.

This is an account of three years' experience in the treatment of Pott's disease in adults using a combination of antibiotics and surgery. The authors give an enthusiastic account of their results, which appear to be very much the same as those reported by workers in this country, using very similar methods of treatment.

JAMES MAXWELL.

Die Tuberkulose im Kindesalter. By E. HUTH. Berlin: Walter de Gruyter and Co. 1956. Pp. 128. Illus. DM 28.

This book aims at a brief survey of our present knowledge of tuberculosis in childhood, and does not pretend to deal fully with the subject. In so far as he goes, the author has done his work well. Quotations, as so often happens, refer occasionally to publications at second hand, for an author cannot be expected to quote original papers which may have been published decades ago. Again, as in so many textbooks, little space has been allotted to chapters that seem important. Such failures seem inevitable in books intended to survey a broad subject. On the other hand, the chapters on progress in diagnosis and treatment are up to date.

S. ENGEL.

BOOKS RECEIVED

The following books have been received and reviews of some of them will appear in subsequent issues.

Price's Textbook of the Practice of Medicine. 9th Edition. Edited by Donald Hunter. London: Cumberlege, Oxford University Press. 1956. Pp. xiv+1,774. 63s. net.

A Textbook of Medicine. 9th Edition. Edited by R. L. Cecil and R. F. Loeb. London: W. B. Saunders and Co. Ltd. Pp. xxxiv+1,786. Illus. £5 5s. net.

Progress in Clinical Medicine. 3rd Edition. Edited by Raymond Daley and Henry Miller. London: J. and A. Churchill Ltd. 1956. Pp. x+424. Illus. 40s. net.

Treatment of Heart Disease. By H. Gross and A. Jezer. London: W. B. Saunders Co. Ltd. 1956. Pp. x+549. Illus. 91s.

Clues in the Diagnosis and Treatment of Heart Disease. 2nd Edition. By Paul D. White. Oxford: Blackwell Scientific Publications. 1956. Pp. xv+190. Illus. 40s.

Cardiology. 2nd Edition. By William Evans. London: Butterworth and Co. (Publishers) Ltd. 1956. Pp. ix+574. Illus. 92s. 6d. net.

Minimal Pulmonary Tuberculosis found by Mass Radiography (Fluorography). By V. H. Springett. London: H. K. Lewis and Co. Ltd. 1956. Pp. xiv+242. Illus. £2 2s. net.

Die Lungentuberkulose. Diagnose und Therapie. By P. G. Schmidt. Stuttgart: Georg Thieme Verlag. 1956. Pp. xii+384. Illus. DM 58.

Supplement 1: *Atlas of Exfoliative Cytology.* By George N. Papanicolaou. Published for The Commonwealth Fund by Harvard University Press, Cambridge, Mass. 1956. London: Cumberlege, Oxford University Press. Illus.

Matters of Life and Death. General Register Office. London: Her Majesty's Stationery Office. 3rd Edition, 1956. Pp. 28. Illus. 1s. net.

The Registrar-General's Statistical Review of England and Wales for the Year 1953. London: Her Majesty's Stationery Office. 1956. Pp. xv+250. 9s. net.

Health Horizon. Edited by Harley Williams. Autumn 1956. N.A.P.T. Pp. 56. Illus. Quarterly: 2s. 6d.

Ireland's Hospitals. 1930-1955. Edited by J. O'Sheehan and E. de Barra. Dublin: Hospitals' Trust (1940) Ltd. 1956. Pp. 78. Illus.

Tuberculosis Control: Plans for Intensified Inter-Country Action in Europe. Report of a Study-Group. World Health Organisation Technical Report Series No. 112. London: Her Majesty's Stationery Office 1956 Pp. 14. 1s. 9d.

Annual Reports of the County Medical Officer. County Council of the West Riding of Yorkshire. For the Year 1955.

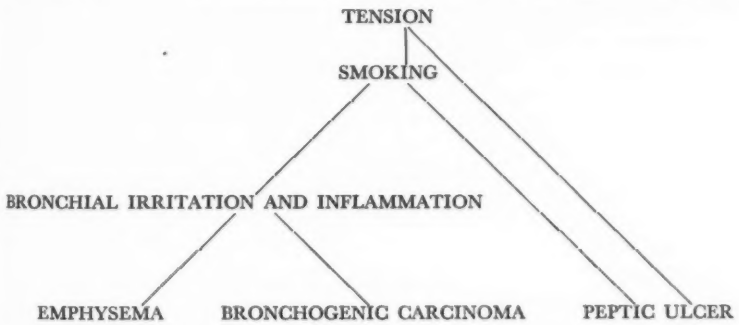
Medizinische Röntgentechnik. (*Medizinischer Teil: Skelettaufnahmen und Organuntersuchungen.*) By Herbert Schoen. Stuttgart: Georg Thieme Verlag. 1956. Pp. xvi+347. Illus. DM 29.70.

REPORTS

NATIONAL TUBERCULOSIS ASSOCIATION OF AMERICA—ABSTRACTS

An association appears to exist, according to Francis C. Lowell, William Franklin, Alan L. Michelson and Irving W. Schiller (*The New England Journal of Medicine*, January 19, 1956), between cigarette smoking and emphysema on the one hand and emphysema and peptic ulcer on the other. They believe that the presence of cigarette smoking in this association is best explained as a cause in emphysema and an aggravating circumstance and possibly a cause in ulcer. Such an assumption, they say, explains the following: the finding that all of a group of 25 patients with emphysema were cigarette smokers of long standing; the reported description of the lesion in emphysema as inflammation and obstruction of the peripheral and narrow portion of the airway; the widely held opinion that smoking aggravates peptic ulcer; the frequency of peptic ulcer in patients with emphysema; and the occurrence, in their group of 25 patients with emphysema, of 3 cases of bronchogenic carcinoma, a disease for which an association with cigarette smoking appears to have been established.

The quantity and manner of smoking (inhalation) or both may be influenced significantly by the personality of the subject, which is here regarded as having a direct bearing in the development of both emphysema and peptic ulcer. A simple plan representing the interrelations postulated is as follows: " Tension " is loosely used to represent a constellation of emotional states and habits ordinarily attributed to those who are anxious, frustrated, ambitious and so forth and who, perhaps because of added factors, may be led or pushed to smoke. Relations other than those indicated may also exist—for example, anxiety produced by respiratory difficulty causing or aggravating ulcer.



The authors therefore suggest that emphysema and perhaps peptic ulcer as well should be assigned a place alongside carcinoma of the lung in the tobacco controversy. Intensive study of this question appears to be warranted, since emphysema as defined above is a disease more common than carcinoma of the lung and has a prognosis almost as gloomy.

N.A.P.T. ANNUAL REPORT, 1955-56

THIS report tells of the activities accomplished by this British voluntary organisation, and it makes very good reading. Among the changes noted is the one in its designation. It is now known as the National Association for the Prevention of Tuberculosis and Diseases of the Chest and Heart, and this widened scope of its activities is timely; for, in addition to the care and attention that it pays to tuberculosis, it is also now cognisant of diseases like chronic bronchitis, lung cancer and heart diseases, and preventive work in diseases of the chest, including cardiology, is now coming within its scope.

Tuberculosis as a world problem is an important feature of the Association's work, and Colonial Scholarships, enabling young men and women from British colonial territories to come to the United Kingdom to study our methods, have been increasingly encouraged since 1954. "Secondment" of doctors to British colonies has also proved to be a valuable link with the dominions. Finally, the Association's voluntary care work is outlined, and the Association is to be congratulated on its multifarious activities.

WORLD HEALTH ORGANISATION

Tuberculosis control: Plans for intensified inter-country action in Europe. Report of a Study Group. World Health Organisation: Technical Report Series, 1956.

This report summarises the discussions of a Study Group convened by the World Health Organisation in order to enable European countries to exchange views on recent experience in tuberculosis control and on the advisability of re-orienting their control programmes, following the rapid decrease in tuberculosis mortality which has occurred in recent years. The Group limited its discussions to pulmonary tuberculosis.

The report first examines the measures to be taken to ensure the comparability of statistical data from different countries. It recommends, *inter alia*, that a precise definition should be given for the terms "case of pulmonary tuberculosis" and "morbidity rate," which are often used with different meanings in different countries. Furthermore, whereas in the past mortality rates have sufficed for estimating and comparing the prevalence of tuberculosis, it is now necessary to have other indices, which might be obtained either from routine health statistics or from special surveys. The establishment in each country of a central tuberculosis register, carefully kept up to date, would be of great value for the epidemiological study of the disease. Among other features it would make it possible to obtain at all times, by an inventory of the register, details of the prevalence of bacillary cases. Should it not prove possible, at least in the near future, to organise a national register, then, to begin with, regional registers could be established which would be gradually extended to cover the whole country. An appendix gives a list of the information which should be collected for each case included in the register.

With regard to the indices which can be obtained from special surveys, the report recommends, on the one hand, the tuberculin index and, on the other, an index based on a complete examination for tuberculosis of sample population groups. The latter index is the more reliable, provided that the groups examined include persons of all ages; an attempt should be made to do this wherever feasible.

Among specific measures for tuberculosis control, case-finding will con-

tinue to play an important part, but the method to be employed will vary according to the country. In regions with low prevalence, the examination of contacts will become increasingly necessary.

The report points out the value of B.C.G. vaccination as a supplementary preventive measure, particularly for the contacts of infectious cases and for highly exposed groups. The control of bovine tuberculosis will become of increasing importance for prevention of the disease in human beings, owing to the relative decrease in the number of infectious human cases.

Hospitalisation of infectious cases will continue to be a major factor in tuberculosis control for a number of years; however, it is to be expected that in Europe the number of beds required for tuberculosis will diminish. The extensive use of new antituberculosis drugs raises the problem of the resistance of the bacilli to such drugs.

Finally, the report stresses the need to encourage the use of rehabilitation facilities, the participation of physicians in the control of the disease, the education of the public, and the provision of social and economic assistance for patients and their families.

NOTES AND NOTICES

REGISTRAR-GENERAL'S STATISTICAL REVIEW OF ENGLAND AND WALES

Commentary on the Vital Statistics for 1953

In this commentary, reference is made to the death rate:

In Tuberculosis. There were 7,913 deaths from respiratory tuberculosis in 1953, compared with 9,335 in 1952 and 17,559 in 1949. The male deaths were a little more than half, and the female deaths rather more than a third, of those in 1949. (The decline in mortality which has continued since 1952 is again reflected in the deaths in 1954, which numbered 7,069.)

In Cancer. Deaths from this cause accounted for 17.7 per cent. of all deaths for males and 17.2 per cent. for females, compared with 17.6 per cent. for each sex in 1952. The increase in the male rate was accounted for by the further increase in deaths from cancer of the lung which numbered 12,881 in 1953, compared with 11,981, 11,116 and 10,254 in 1952, 1951 and 1950 respectively. Most of this increase occurred between the ages 65 and 84.

In Influenza. There was a mild outbreak of influenza in the first quarter of the year and 6,465 deaths were assigned to this cause, compared with the low figure of 1,750 in 1952. The deaths occurred mainly among persons aged 45 years and upwards.

THE THORACIC SOCIETY

The Spring Meeting, 1957, will be held on Friday and Saturday, March 1 and 2, 1957, at the Royal College of Surgeons, London.

The Summer Meeting will be held in Newcastle upon Tyne on Friday and Saturday, July 5 and 6, 1957.

N.A.P.T. SYMPOSIUM ON CHRONIC BRONCHITIS

An interesting symposium on chronic bronchitis was held at B.M.A. House on Wednesday, December 12, with Dr. J. L. Livingstone in the chair. The subject was introduced by Dr. Neville Oswald; Morbid Anatomy, Infection in the Ætiology of Bronchitis, Air Pollution and Chronic Bronchitis, Diagnosis, Radiology, Clinical Management, the Place of Bronchitis in Thoracic Surgery, Geriatric Aspects and the Social Care and Administrative Aspects all received attention; and Miss Lynne Reid, Dr. J. R. May, Dr. P. J. Lawther, Dr. C. M. Fletcher, Dr. George Simon, Dr. Joseph Smart, Mr. J. R. Belcher, Dr. Frank Cooksey and Dr. Trevor Howell were among the speakers introducing the various aspects outlined.

AMERICAN TRUDEAU SOCIETY

The 52nd Annual Meeting of the American Trudeau Society, medical section of the National Tuberculosis Association, will be held in Kansas City, Missouri, May 6 to 9, 1957, in conjunction with the annual meeting of the National Tuberculosis Association.

In addition to scientific sessions at which papers will be presented on current research, plans are being made for seven special lectures and four panel discussions. Topics for the latter will be tuberculin testing, fungous diseases, tuberculosis case finding, and the surgical approach to the bad chronic case of tuberculosis.

The lectures will be on cor pulmonale, chest injuries, hazards of radiation, tuberculosis in animals, histological studies in smoking, mucovisidosis, and diseases of the diaphragm.

PROFESSOR CHARLES SINGER'S EIGHTIETH BIRTHDAY

Professor Charles Singer, Emeritus Professor of the History of Medicine in the University of London, celebrated his eightieth birthday, on November 2, last.

He has been a valued contributor to this Journal on several occasions, and we send him our sincere congratulations and good wishes.